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Editorials . . .

NEW CLINICAL FACILITIES

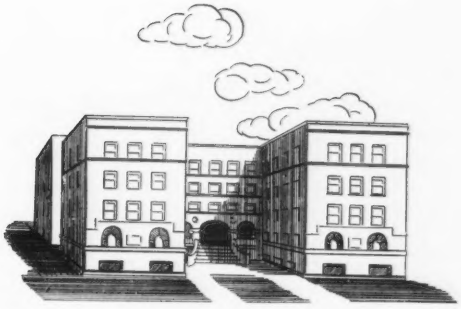
In these pages will be found an announcement that The Chicago Medical School has affiliated with the Mount Sinai Hospital of Chicago, having already become effective at the beginning of this academic year. Such an association provides for clinical facilities for the teaching of our junior and senior classes, and the formation of a teaching hospital. Clinics, classes, seminars, all provide our students with the latest knowledge and experience, keeping them abreast of medical progress, resulting in better doctors.

The Mount Sinai Hospital is one of the largest in Chicago, with an extensive out-patient department (having now absorbed the clinic formerly conducted by the School), as well as several hundred beds and other fine departments. It was founded in 1918 as a non-profit organization dedicated to the service of the community. Subsequently it has become affiliated with the Community Fund and Jewish Charities of Chicago. Since its inception the hospital has been constantly building and expanding its facilities. The hospital is attended by some of Chicago's most outstanding physicians, many of whom have been appointed to the teaching staff.

Another hurdle in the advance of The Chicago Medical School has been cleared. Due to the impetus given us last spring by the Council on Medical Education and Hospitals of the American Medical Association, our institution can now be proud of its clinical affiliation with a fully approved hospital. Both of these institutions will be enhanced by the association with one another, and even greater benefits will be received by Chicago and the nation.

The Staff

THE INDIVIDUAL AND DISEASE



A great deal has been written about the mind, the psyche, and the nervous system as the etiological factor in the causation of many diseases about which we know little; e.g., ulcerative colitis, peptic ulcer, leukemia, etc. It is undoubtedly true that the nervous system affects the disease process, including its etiology, just as it affects the normal functioning of every organ and tissue in the body. What many physicians fail to realize, however, is that the psyche plays a prominent role not only in the etiology, but also in the course, treatment and prognosis of disease.

It has long been, and still is, a practice in the teaching of medicine to emphasize treatment of the disease per se; and now, with the advent of chemotherapy and the antibiotics, it is becoming more of a practice to use those drugs at the first sign of any abnormality without being aware of the nature of the abnormal process.

It is believed by many that the patient's mental state affects the production and manifestation of disease (any abnormality or deviation from the "normal", or healthy state), to a large extent through the reactive processes of his body.

Treatment, then, should be in accord with this concept. White (1) points out that in the management of hypertension the patient should be made aware of his disease, thus creating more cooperation, and, in turn, better results. Good treatment is the product of full understanding of the disease, and, in any case, the psychological factor, as well as the organic bases must be considered to get a complete picture.

This psychological awareness, this treatment of the patient as an individual personality and not merely as a cardio-vascular or gastro-intestinal system, should be the practice of every conscientious physician. The old adage is still applicable: *Treat the individual, not the disease.*

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(1) White, P.D., Management of Hypertension; Annals of Internal Medicine, 27:5, Nov. 1947.

THE AIMS CONVENTION

There has not yet been time to receive, correlate, and comment on the annual convention of the Association of Internes and Medical Students. By the next issue we shall endeavor to evaluate this most successful meeting.

RECENT TRENDS IN THE TREATMENT OF PERIPHERAL VASCULAR DISORDERS*

DAVID I. ABRAMSON, M.D., F.A.C.P.**

ONLY RECENTLY has the subject of peripheral vascular disease emerged as a separate and distinct specialty. Previously, treatment of vascular disorders consisted of alleviating symptoms through surgical means; now the emphasis is placed upon the early recognition of the condition, at a time when the pathologic changes are still reversible and hence amenable to medical therapeutic procedures.

The field of vascular disorders can be grossly divided into three catagories: arterial, venous, and lymphatic; depending upon what part of the vascular system is predominantly involved. The following is a discussion of the most common peripheral vascular disorders and the application of treatment as we understand it today.

Diseases of the Arteries

Organic:

The type of treatment used depends on the stage of the disease. Regardless of the severity of the condition, little success can be anticipated with any procedure, whether surgical or medical, if the patient continues to smoke. This is particularly true with regard to thromboangiitis obliterans, and to a lesser extent, to arteriosclerosis obliterans. In thromboangiitis obliterans the type of response to smoking bears a certain resemblance to a hypersensitivity phenomenon in the sense that even an occasional cigarette is sufficient to cause progression of the disease. In arteriosclerosis obliterans smoking probably has its deliterious effect through its vasoconstricting action alone.

If the main complaint is intermittent claudication, indicating a reduction in the circulation to the muscles of the leg or the small muscles of the feet, without any signs suggesting a decrease in the cutaneous circulation . . . that is, if there are no trophic disturbances, in my opinion, the therapy should be entirely medical. There is little, if any, physiological or clinical basis for sympathectomy under these circumstances.

Abstinence from smoking, alone, will frequently cause an improvement in the ability to walk; or at least it will prevent or slow the progress of the disease. This is particularly true of thromboangiitis obliterans and to a much lesser extent, of arteriosclerosis obliterans.

The prolonged use of pancreatic extracts as Padutin and Depropanex will not infrequently produce a definite increase in the ability to walk. This is seen more often in cases of arteriosclerosis obliterans, and much less frequently in thromboangiiti obliterans. An adequate trial of the efficacy of the extracts is a three week period with two to three intramuscular injections weekly. If a definite improvement has not occurred at the end of that period, further administration will probably not alter the clinical picture. If there is a definite increase in the ability to walk, the therapy should be continued at less frequent intervals.

The exact basis for the therapeutic effect noted with the use of pancreatic extracts is not clear. There is little doubt that these substances do not produce immediate vasodilation. It may be that the action is related to an increase in the collateral circulation, with a consequent augmentation of the blood supply to the muscles of the calf and foot; or it may be due to an improvement in the metabolism of the ischemic muscles.

Some workers have advocated the use of hypertonic saline solutions, administered intravenously, in the treatment of intermittent claudication. It is necessary to give the injections one to three times weekly for at least a year or longer before we can expect some benefit from the therapy. It is obvious that the practical aspects of the program, from the point of view of time lost and expense to the patient, must be considered before undertaking this procedure. Furthermore, the excellent results reported by the workers who have publicized this method have not been duplicated by others.

If the patient complains of symptoms at night which fall into the category of ischemic neuritis, such as various types of paresthesias, burning, and lancinating pain, narcotics may be necessary.

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* Lecture delivered at the Chicago Medical School, October 15, 1947.

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It has been reported that in patients with a reduced peripheral circulation, the peripheral nerves in the legs show Wallerian degeneration and fibrosis. The symptoms experienced by these patients at bed rest may be on this basis. There is little difference between them and those experienced by a diabetic with peripheral neuritis. Thiamine chloride in large quantities may at times reduce the pain considerably. If the patient complains of night cramps it is worthwhile to give him some quinine before retiring. The mode of action here is not known, but it may have something to do with altering the metabolism of the muscles.

When the obliterative arterial vascular disease has progressed to the point of inadequate circulation for the tissue needs even at rest, then trophic disturbances such as ulceration or gangrene appear. The symptom of intermittent claudication is now relegated to the background and therapy is aimed at increasing the cutaneous circulation in an attempt to heal the lesion. To this end medical treatment should be given a trial before resorting to surgery. This embraces those procedures and drugs giving vasodilatation. Included in the latter are a pair of relatively recent drugs which appeared in the literature: tetra-ethyl-ammonium blocks the transmission of nerve impulses through all autonomic ganglia, while Dibenamine acts to paralyze temporarily those sympathetic nerve endings at which adrenergic substance is produced. Thus the vasoconstricting impulses are blocked, allowing the vessels to dilate. The action is relatively prolonged with the use of Dibenamine and may last for 24 hours or more. Foreign protein therapy (typhoid vaccine), intermittent venous occlusion, Buerger's exercises, and the Sanders' bed may be useful adjuvants to the other procedures.

If, after extensive treatment with the various medical procedures, no definite improvement is noted in a three week period, then surgical intervention should take place. Sympathectomy should should now be seriously considered. Not infrequently ulcerations which have not healed with medical treatment will show rapid and definite improvement after sympathectomy.

The most important point in the treatment of sudden or gradual occlusion of large arteries as by an embolus or a thrombus, is the early diagnosis. If the diagnosis is made within two to five hours, the best treatment is first medical and then embolectomy, provided the clot has lodged in the femoral or popliteal arteries. Heparin, intravenously, should be started as soon as the diagnosis is made; in addition dicumarol should be given. The reflex spasm of the collateral vessels, which almost invariably occurs when a large artery is suddenly occluded, should be treated by the common vasodilating procedures. Should the diagnosis be made later than 8-10 hours after the onset of the condition the various vasodilating procedures should be utilized, but an embolectomy is generally unwarranted.

The treatment of a thrombus in a major vessel is similar to that described for embolus with the exception that removal of the clot is **never** performed.

Functional:

The type of treatment in Raynaud's disease depends on whether or not nutritional disturbances are present. In those instances in which there are no trophic manifestations, the important point with regard to therapy is protection from cold and sudden changes in temperature. Warm clothing is especially helpful. If the patient continues to have repeated attacks despite precautions, it may be necessary for him to move to a warm climate.

In those individuals in whom nutritional disturbances are present, such a thickening of the skin with loss of subcutaneous tissue, or ulceration and gangrene of the tip of the toes or fingers, or in whom the attacks of color changes are so frequent or so severe as to be incapacitating, sympathectomy is generally indicated. However, this type of treatment is necessary in only a small percentage of cases of Raynaud's disease. The reponse of nutritional disturbance to sympathectomy is frequently quite spectacular. Within two or three weeks after operation, ulcerations which have persisted for years may clear up entirely.

With regard to treatment of acrocyanosis, there is usually none necessary, since the condition has no serious complications. By reducing exposure to cold to a minimum, the severity of the disease can also be decreased. The prognosis is good.

Erythromelalgia, a rare functional disorder, is treated, for the most part, symptomatically. For reasons which are not clear, the symptoms may respond well to aspirin. Avoidance of a warm climate may help to minimize the attack.

In most instances treatment of livedo reticularis is not necessary since the symptoms are

mild. The patient should be protected from cold in this condition. Sympathectomy has been suggested in the severe cases, but unless ulceration is present the procedure is inadvisable.

Diseases of the Veins

Considerable difference of opinion exists with regard to the treatment of superficial and deep thrombophlebitis. In the case of simple benign superficial thrombophlebitis, some workers advocate the application of an elastic bandage starting above the proximal level of the thrombosed segment and covering the entire extremity below it. The patient is then allowed to become ambulatory. Others still adhere to the conservative treatment, consisting of bed rest, elevation of the involved extremity and continuous application of moist heat locally. Generally there is no indication for the use of dicumarol. However, it must be pointed out that the word "benign" is used advisedly in this case, since superficial thrompophlebitis may be followed by breaking off of thrombi and their lodgement in the pulmonary vessels. Therefore if there are signs of rapid upward propagation into the greater saphenous vein in the direction of the fossa ovalis, ligation and section above this level are indicated.

Opinion as to the treatment of deep thrombophlebitis is even more diverse. There are some who advocate vein ligation, particularly in the case of phlebothrombosis or if an embolus has broken off and produced a pulmonary infarct. These workers generally advise ligation not only on the involved side, but also on the opposite, apparently normal, extremity; on the basis that the process is bilateral, despite the fact that the symptoms exist on only one side. Ligation of the iliac veins and inferior vena cava have been performed. There are others who advocate repeated paravertebral procaine blocks in an attempt to remove the associated vasospasm. Some utilize a combination elastic bandage applied around the entire extremity, and then advise the patient to become ambulatory at once. The conservative method consists of rest in bed, elevation of the extremity, application of moist heat and symptomatic treatment of complaints. It is my opinion that in the case of the patient suffering from his first attack of deep thrombophlebitis, the conservative treatment is adequate if supplemented with anticoagulant therapy and the early use of Dibenamine to remove vasospasm. Heparin and dicumarol should be given simultaneously and then the heparin discontinued after the second day, while the dicumarol should be continued for at least one week after the patient becomes ambulatory again. If despite such precautions a pulmonary embolus occurs, then ligation and section of the main vein of the involved extremity should be carried out.

Syndromes Following Exposure to Cold

In addition to the vascular disorders noted, another group of disorders may be discussed. These are those vascular abnormalities associated with war. Of greatest importance, because of the great number of soldiers usually affected, is trench foot.

I shall not attempt to discuss the early treatment of the condition since such a problem never arises in private or hospital practice. However, the sequelae of trench foot are being seen more and more often. For those cases with frank loss of tissue, the treatment involves the use of proper prosthesis. In the great majority of cases the complaints consist of pain in the sole of the foot which prevents the individual from walking and signs of marked responsiveness to extremes of temperature. The use of a double heel may be of aid in counteracting the pain in the sole of the foot by shifting the weight of the body from this sensitive portion to the area in front of the heel. Very little can be done to counteract the symptoms that occur when the feet are exposed to extreme heat or cold except to minimize exposure to such extremes. If excessive sympathetic tone is the predominant abnormality, sympathectomy may be attempted to counteract the marked hyperhydrosis, coldness and cyanosis This procedure will generally not help the pain in the foot and it is questionable whether it is indicated for the purpose of removal of vasospasm and hyperhydrosis alone. Time will probably take care of most of the symptoms.

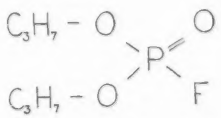
In the case of high altitude frostbite and the common variety of frostbite, moisture plays only a small role. The tissues are actually exposed to an environmental temperature definitely below freezing. Many of the points in the treatment of the early stage remain controversial. The frozen extremity should be carefully protected and not subjected to trauma, not even gentle massage. Sterile dressings should be applied over any existing or potential breaks in the continuity of the skin. There is some question as to whether to

(Continued on page 34)

PHYSIOLOGICAL PROPERTIES OF DI-ISOPROPYL FLUOROPHOSPHATE (DFP) AND POSSIBLE CLINICAL APPLICATIONS

PIERO P. FOA, Ph.D., M.D.*

THE alkyl fluorophosphates have been first described by Lange and Krueger in 1932 (1). Their interest for the physician lies in the fact that these compounds have strong cholinergic properties and are sufficiently toxic to have been suggested as possible agents for chemical warfare. Perhaps the most toxic compound of the series is di-isopropyl fluorophosphate (DFP) which can be lethal by inhalation and, in doses small enough to be undetected, has powerful knock-out and miotic actions. DFP is a clear, colorless liquid, slightly soluble in water and soluble in organic solvents. It has the following formula:



Other, less toxic compounds of the series have been suggested as insecticides, fungicides and bactericides (2). A vapor concentration of 0.44 grams of DFP in one cubic meter of air will kill 50% of the mice exposed to it (LC50). Death will occur within 30 minutes in most cases (2). The lethal dose which will kill 50% of the animals (LD50) when injected intravenously is 0.34mg/kg for the rabbit and 1.6mg/kg for the cat. The animals will die after a period of muscle tremors and spasticity, of excitement and convulsions followed by a complete paralysis of the muscles of the neck and, gradully, of the whole body. These effects are similar to those produced by nicotine. The animals further show a series of symptoms similar to those produced by muscarine, such as miosis, salivation, bronchorrhea, increased gastrointestinal motility and diarrhea. It will be noted that the syndrone just described in very similar to that produced by acetylcholine which also has both "nicotinic" and "muscarinic" actions. The similarity between the action of acetylcholine and that of DFP is not accidental and it is due to the fact that DFP inhibits the cholinesterase of the blood and tissues so that the acetycholine formed during normal physiological activities is not immediately destroyed. This property of DFP is very similar to that of physostigmine, but, contrary to the latter, it persists for long period of time.

The anticholinesterase properties of DFP have been studied by Mazur and Bodansky (3). These authors measured the cholinesterase activity of serum, blood cells and tissues of the rabbit, monkey and man by determining the amount of CO_2 liberated from added bicarbonate by the acetic acid set free during the destruction of acetylcholine. The inhalation of DFP produced a lasting and marked reduction of the cholinesterase activity in all experimental animals. Fifteen men were exposed to DFP vapors for periods of time varying between 8 minutes and 42 seconds and 10 minutes and 40 seconds. The vapor concentration in the inspired air varied from 19 to 28.8 micrograms of DFP per liter. The symptoms were very mild and consisted of miosis and tightness of the chest lasting for several hours and, occasionally, nausea, salivation and rhinorrhea.

In spite of the amounts of DFP inhaled and the mildness of the symptoms, the cholinesterase activity of the serum was promptly reduced to from 1 to 5 per cent of normal and was still only 70 per cent of normal 15 days after exposure. The inhibition of the cholinesterase activity of rabbit brain persists even longer and is still reduced 50 days after exposure to DFP. Apparently DFP forms a very stable compound with cholinesterase or destroys this enzyme. This is demonstrated also by the fact that dialysis does not reactivate the serum, whereas it does so when the latter had been inactivated by physostigmine. The action of physostigmine itself lasts only about 2 hours (4). The sites of action of DFP in the intact animal are probably at the autonomic neuro-effector organs, at the ganglia or at the myoneural junctions where acetylcholine is usually produced and immediately destroyed. The gradual disappearance of anticholinesterase activity in the intact animals or in the isolated tissues is due to the hydrolysis of DFP into inactive products. This hydrolysis occurs mainly

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in the liver, although the plasma and the kidney contain a measurable amount of hydrolytic enzyme. The latter was isolated and studied by A. Mazur (5).

The inactivation of tissue cholinesterase by DFP made possible the study of the pharmacological properties of physostigmine other than that of inhibiting cholinesterase (6). It was found that physostigmine has a strong cholinergic action which persists also after all cholinesterase activity is blocked by DFP. Furthermore, it was found that physostigmine has a curare-like action on cat muscle very similar to that of acetycholine. On the other hand, R. Koster (7) demonstrated that physostigmine, protects cats against the toxic effects of subsequent doses of DFP. The lethal dose of the latter is increased 3 to 6 times. If the animal is atropinized, larger doses of physostigmine can be administered and the animal can tolerate 30 LD50's of DFP. On the contrary if physostigmine is given after DFP its action is enhanced. The increased susceptibility of the DFP treated animal to physotigmine is probably due to the destruction of cholinesterase by DFP. It appears that the mechanism of action of physostigmine is similar, but not identical with that of DFP.

The action potentials of nerves and nerve end plates seems to be associated with the liberation of acetycholine. According to this theory acetycholine would depolarize the membrane of the nerve cells allowing the conduction of the nerve impulse. The function of cholinesterase would be that of destroying acetycholine, repolarize the membrane and interrupt the activity of the nerve. A confirmation of this theory was given when it was found that DFP completely abolishes the action potential of nerves (8) and muscle (9).

The similarity between the pharmacological action of DFP and that of physostigmine suggests that DFP might have therapeutic applications with the added advantage of its prolonged action. The toxicity of DFP is very marked and, before the drug could be used clinically, it was necessary to find a way of counteracting it. As we have seen, DFP has both nicotine and muscarine actions and no single drug is known which is capable of blocking both these effects. Atropine is highly parasympatholytic in clinical doses and is capable of counteracting the muscarinic effects of acetycholine; however agents which block nicotinic actions are very difficult to control. Attempts to mask the nicotinic action of DFP with curare were not successful (10). Magnesium salts have curare-like action and a combination therapy with atropine and magnesium sulfate was successfully attempted. It was found that it actively counteracts the effects of DFP also after the effects of the drug have become manifest. The experiments were performed on rabbits receiving DFP by intravenous injection or by inhalation and magnesium sulfate and atropine by intramuscular injection. Magnesium sulfate was given in the dose of 800mg/kg, atropine sulfate in the dose of 20mg/kg. The use of magnesium salts should be guarded when flaccid paralysis has already set in, because the symptomatology becomes more severe and the animal may die suddenly. Furthermore, the bronchoconstrictive effect of DFP is not prevented by magnesium and atropine and may have to be treated with epinephrine or aminophylline (10). The magnesium salt probably acts by antagonizing the nicotinic effect of DFP, this explanation, however, is not completely satisfactory because other metals (calcium, aluminum and gold) give some protection against DFP without having any curare-like action and without abolishing muscle tremors (11).

A solution of DFP in triacetin or in propylene glycol instilled into the eye of a rabbit produces maximal miosis lasting for 24 hours or more. This period of miosis is followed by another 24 hour period during which the pupil reacts very sluggishly. Successive applications of the drug at 24 hour intervals produce no cumulative effects. Large doses produce irritation of the conjunctiva and undiluted DFP is very toxic. A dose of 1.4mg/kg in the conjunctival sac kills the animal rapidly (12). The lasting miotic effect of DFP was used in the treatment of glaucoma (13). It was found that an installation of DFP solution in human eyes produced prolonged miosis (6-27 days), ciliary spasm and false miopia (2 days) and decreased intraocular tension (4-8 days) without any local irritation. One or two instillations of 0.1 or 0.2% DFP overcame and outlasted the cycloplegic effects of 4% homatropine and 1% atropine. DFP was used in the treatment of 76 glaucomatous eyes in 52 patients previously treated with physostigmine or pilo-

carpine. The intraocular tension was reduced and maintained to normal even in those cases in which the other miotics had little or no effect. Further loss of visual field was prevented. In most cases one instillation every 1 to 10 days was sufficient to maintain the therapeutic results. No systemic effects were noted, although in some instances there were visual blurring, eye ache and spasm of accommodation.

The physostigmine-like action of DFP suggests that this drug might be useful in the treatment of myasthenia gravis. This was tried with encouraging results (14). When 1.5 mg of DFP in 3 cc. of saline were injected into the brachial artery there resulted a striking localized increase in muscle strength and the characteristic pathologic changes in the electro-myographic records disappeared. The local increase in muscle strength remained detectable for 8 to 10 days. Another series of patients with myasthenia gravis was given DFP by intramuscular injection or by mouth (15). Seven patients received 2.5 to 210 mg. of DFP over a period of 1 to 150 days. The effectiveness of DFP was compared with that of neostigmin by a series of objective dynamic and static muscle function tests and by electromyograms. DFP relieved muscle weakness for longer periods of time than physostigmine, but never to the same degree.

It is too early to evaluate the therapeutic value of DFP in cases of glaucoma and myasthenia gravis. The results obtained to date are, however, very promising and it is possible that other applications of the drug may be found in the future, especially when a prolonged stimulation of the parasympathetic nervous system is desired.

BIBLIOGRAPHY

1. Lange, W. and Krueger, G.: Ber. Chem. Gas. 1932, *65*, 1598.
2. McCombie, H. and Saunders, B. C.: Nature 1946, *157*, 287.
3. Mazur, A. and Bodansky, O.: J. Biol. Chem. 1946, *163*, 261.
4. Kerr, W. J. and Whipple, G. H.: Amer. J. Physiol. 1919, *47*, 356.
5. Mazur, A.: Feder. Proc. 1946, *5*, 147.
6. Riker, W. F., Wescoe, W. C., Cattell, McK. and Shorr, S.: Feder. Proc. 1946, *5*, 198.
7. Koster, R.: J. Pharm. & Exp. Ther. 1946, *88*, 39.
8. Bullock, T. H., Grundfest, H., Nachmansohn, D., Rothenberg, M.A. and Sterling, K.: J. Neurophysiol. 1946, *9*, 253.
9. Couteaux, R., Grundfest, H., Nachmansohn, D. and Rothenberg, M. A.: Science 1946, *104*, 316.
10. McNamara, B. P., Koelle, G. B. and Gilman, A.: J. Pharm. & Exp. Ther. 1946, *88*, 27.
11. Modell, W. and Krop, S.: J. Pharm. & Exp. Ther. 1946, *88*, 34.
12. Scholtz, R. O.: J. Pharm. & Exp. Ther. 1946, *88*, 23.
13. Leopold, I. H. and Comroe, J. H., Jr.: Feder. Proc. 1946, *5*, 190.
14. Harvey, McG. A., Jones, B. F., Talbot, S. and Grob, D.: Feder. Proc. 1946, *5*, 182.
15. Comroe, J. H., Jr., Todd, J., Gammon, G., Koelle, G. B. and Gilman, A.: Feder. Proc. 1946, *5*, 172.

New Books in the Library

Cook, D. Ulcer, primary cause of gastric & duodenal ulcer. c1946. 2 copies. 23 J C 77 (The author an alumnus of C.M.S.)

Cooke, R. A. Allergy. 1947. 8 G C 77

Gesell & Amatruda. Embryology of behavior. 2d ed. c1945. 26 Ng C 33

Hamilton, Boyd & Mossman. Human embryology. 1945. 3 G H 18

Katz, L. N. Electrocardiography . . . with atlas. 2d ed. c1946. 15 E K 15 Exercises in electrocardiographic interpreations. 2 ed. c1946. (These are gifts from the "Quarterly".)

McGuigan & Krug. Materia medica & pharmacology. 2d ed. 1940. 22 C McG

Mason & Zintel. Preoperative & postoperative treatment. 2d ed. 1946. 23 L M 38

Peters & Van Sylke. Quantitative clinical chemistry, vol. 1 2d ed. 1946. 5 A P 44

Pullen, R. L., ed. Medical diagnosis applied physical diagnosis. 1946. 7 D P 96

Ricci, J. V. One hundred years of gynecology, 1800-1900. c1945. R 33

These books are in the show case and may be consulted by applying to the Librarians.

A.M.A. New & non-official remedies. 1946. 22 D Am 3

Amer. Nat'l Red Cross. Service record. 1939-1946. 1946. 42 Am 51 r

American women. 1937. 1 E Am 3

Bacon, H. E. Anus, rectum & Sigmoid colon. 2d ed. c1946. 16 J B 13

Benda, C. E. Mongolism & cretinism. 1946. 14 V B 43

Brookes & Alyea. Poisons. c1946. 34 P B 79

Brunschwig, A. Radical surgery in abdominal cancer. c1947. 13 V B 83

Castle & Minot. Pathol. physiol. & clin. description of the anemias. 1945. 14 C C 27

COMPLICATIONS OF SPINAL ANESTHESIA

IRVING H. BLUMENFIELD, B.S., M.D.

(Continued from last issue—conclusion)

Respiratory Depression and Failure

I have noticed very little respiratory depression that could be directly related to the method (refer to Part I). The depression that is seen is usually at a maximum preliminary to any procedure and is due to the premedication with opiates and barbiturates. Many of the patients are even slightly cyanotic due to hypoventilation, but there seems to be no ill effect from this.

In our work we avoid high spinal as much as possible and this helps us in eliminating respiratory depression as a factor. If high abdominal operation is to be done, we utilize or hold in readiness all the prophylactic measures in our armamentarium. The level is effectively controlled so that we do not involve the phrenics or highest intercostals; prophylactic ephedrine sulphate is administered to avoid medullary anoxia; and oxygen is administered during the course, if indicated, or even prophylactically.

Depression and paralysis of the respiratory center during spinal anesthesia is due to blockage of the innervation of the intercostals and phrenics—and not the direct effect of the novocaine on the center. Although the respiratory center can be directly affected by absorption of some of the agent through the blood stream, this can be avoided with a due amount of caution.

Koster (7b) restated the well known pharmacological fact that novocaine has six times the affinity for the sensory nerves as for motor nerves. "It is now not so difficult to understand how respiratory movements initiated by a purely automatic center may be maintained despite the existence of such a degree of poisoning by an anesthetic as has brought about an interruption of conductivity in sensory fibres. It is this property of selectivity (dependent upon inherent differences in nerve fibre endings and cells) which is so important a factor in the explanation of the phenomenon of surgical anesthesia of the entire body without respiratory paralysis. Thus, it becomes apparent that, in the average case of spinal anesthesia, in which no fatality has resulted, the lack of respiratory paralysis is not due to any particularly good fortune, whereby there has been too little diffusion of the anesthetic toward the medulla in sufficient concentration to cause the dreaded effects, but rather to the fact that the respiratory center is a station for the initiation of motor impulses and possesses, inherently, properties that render it immune to the effects of an anesthetic in the concentration advocated for spinal anesthesia."

We do not rely on this fact clinically and attempt, unlike Koster, to control the level of our anesthetic agent.

Cardiac Arrest

This is very rarely reported and is due to blocking of the cardiac accelerator nerve. Koster (7c) in the five per cent of his cases wherein the alarmed anesthesiologist could feel no radial pulse or register any pressure by the manometer —would reassure him during the course of any intrabdominal operation by feeling the abdominal aorta in which slow, regular pulsations could be distinguished. No need to delve further into this since, with our modern refinements of technique, it is rarely encountered.

Complications Following Spinal Headache

The most troublesome and frequent complicationf of spinal anesthesia is headache. Modern technique has reduced its incidence so that its occurrence is less frequent than after the administration of ether (5c). The theories for its cause are many but its pathogenesis is not actually understood. Some of the theories are:

1—Loss of cerebrospinal fluid through the puncture wound in the dura by seepage into the extradural soft tissues.

2—Meningeal irritation—by reflex stimulation with ensuing dilatation of cerebral vessels, or by

3—An increase in the volume of cerebrospinal fluid contained within the subarachnoid space.

4—Too early elevation of head (although some now advocate this).

5—Stimulation of cord proper by needle inserted too deeply.

6—Injection of air with the anesthetic solution.

7—P.H of cerebriospinal fluid.

8—Contamination of the material injected, causing irritation of nerve tissue.

The mechanism of occurrence in the first instance has been ascribed to the lack of elastic and contractile tissue in the fibrous dural membrane. It is believed that the puncture hole caused in the dura by the needle point does not close until a fibrin clot forms. Castro Silva (13) states that it has been his lot to perform laminectomies eight or fifteen days after a lumbar puncture and to find the tracts of the puncture still gaping, closely simply by non-adherent, epidural fat.

Upon the withdrawal of the needle, the dura and the underlying pia-arachnoid are left in one of two possible relations. Either the openings in the two membranes are superimposed, if the pia is drawn back through the dural opening by the needle, allowing leakage to take place, or else the movement of the soft membranes upon each other causes the openings in the respective membranes to be situated at different levels. The force of the cerebrospinal fluid is then thought to compress the pia-arachnoid against the dura for an interval long enough to permit the pial opening to close by virtue of its inherent elasticity. If the latter mechanism takes place very little spinal fluid will escape.

As a result of the considerable seepage of spinal fluid during the first few hours after the operation, there is a disturbance of the intracranial portion of the cerebrospinal fluid. It has been explained that the latter factor, by removing the watery cushions, allows the brain to sag against the bony framework of the skull. This, in turn, supposedly, irritates the dural fibres of the trifacial and the two occipital nerves. Pressure upon the basilar venous plexus diminishes the outflow of venous blood from the cranial cavity and brings about an increase of venous tension. This lowering of the patient's head is thought to remove the brain from contact with aforementioned nerves and venous plexus, and thus tend to lessen the severity of headache. Relief is similarly obtained when the opening in the dura has closed, seepage of fluid has ceased, and the normal watery cushion of the brain has been restored.

Koster et al, did not believe that the following are factors in causing headache,—contamination of antiseptic solutions used for sterilization of skin (needle puncture through skin dripping with iodine); hypertonicity resulting from dissolving crystals of procaine hydrochloride in cerebrospinal fluid. This has been shown, clinically, in a group of patients.

The majority of the patients afflicted with headaches begin to complain, as a rule, within the first twenty-four hours after the operation. Usually the headache is throbbing, either occipital or parietal in location, and is frequently associated with some degree of stiffness of the neck muscles, tinnitus, diplopia, etc. The intensity varies. In most instances the discomfort is so mild that the administration of either aspirin or an A.P.C. capsule or the application of an ice cap suffices. Rarely is the suffering of such great intensity that the usual analgesics are of no avail. In both the mild and severe grades the headache seems worse when the head and shoulders are raised (although some discount this fact). Relief is usually maintained in the former type by maintaining the horizontal position.

It is well not to question the post-operative patient concerning the presence of headache. The answers will usually have a plurality of affirmatives as the patient is so psychologically predisposed to accept extra care and sympathy. We should await an unsolicited statement of this symptom to make it reliable. To be considered also are history of migraine, hypertension, eyestrain and other predisposing causes of headache.

Postspinal headache is considered an important complication of lumbar puncture.

Post Operative Urinary Retention

The hypothesis that the anesthesia induction produces a localized serous meningitis and this disturbs the anal and vesical spinal centers in the lumbar region of the cord is contraindicated by the statistical evidence demonstrating the approximately equal frequency or in some reports the greater frequently following inhalation anesthesia.

Surgical procedures involving the lower abdoman, inguinal regions and perineum are associated with a high incidence of postoperative urinary retention because of their proximitty to the urinary bladder (ref. 14). Essentially the disturbance is one of the trauma to the bladder

innervation due to operative manipulation. Spinal anesthesia slightly diminishes urinary secretion indirectly because of the lowered blood pressure. It is of short duration and usually easily managed with some psychotherapy, prostigmine and catheterization if necessary.

The Clinical Aspects of Pulmonary Atelectasis

The conception of some surgeons that any anesthetic which is not inhaled is safe for the lungs is fallacious (ref. 15-16). Atelectasis which follows operations under various regional procedures occurs about as frequently as following general anesthesia. Here, the factors which operate are different. During operations under local, regional or spinal anesthesia it is usually necessary to give large quantities of sedatives to patients in order that they should not become restless especially if the operation is time consuming. Non-volatile drugs in larger amounts interfere with normal respiratory physiology producing central depression. If to this are added the ineffectiveness of the cough reflex and paralysis of at least one-half of the inter-costal muscles, under spinal anesthesia, for an effective abdominal block; a change of diaphragmtic action of post-operative musclesplinting as a result of pain, the conditions for bronchiole stasis with obstruction and atelectasis are ideal. Practically, the anesthesiologist has less control than under inhalatiton anesthesia. He can only hope to prevent atelectasis by the judicious use of sedatives plus frequent instruction to the patient to take deep breathing.

Lyford's (ref. 17a, b) findings are worth noting. Six hundred and thirty-one cases in which abdominal operations were performed under ether, cyclopropane or spinal anesthesia on patients without infections of the respiratory tract at the time of operation were reviewed to determine the incidence of post-operative infections of the respiratory tract with each type of anesthesia. It was found that approximately the same proportion of patients without infections of the respiratory tract acquired post-operative infections of the respiratory tract with inhalation and with spinal anesthesia; i.e., the incidence was with ether anesthesia 5.8 per cent, with cyclopropane anesthesia 4.9 per cent, and with spinal anesthesia 7.5 per cent.

Another 120 cases, who had been shown to have low grade, chronic pre-operative infections of the respiratory tract of the kind not generally considered contraindications to even elective operations, were analyzed. These patients had acute post-operative infections of this tract approximately two and one-half times as frequently as after inhalation anesthesia, i.e., the incidence was after ether anesthesia 13.5 per cent, after cyclopropane 17.5 per cent and after spinal anesthesia **39.5 per cent.**

It can be readily seen that atelectasis and other pulmonary complications are factors to be respected and guarded against in spinal as well as inhalation anesthesia. The atelectasis if not controlled will develop into a pneumonia. Moreover, the disposition toward pneumonia and other pulmonary complications is in direct proportion to the complexity of the surgical procedure and the condition of the patient. The anesthetic agent is just another factor involved. The spinal method is no greater offender than any other. Proper medical and nursing care will do much to prevent these respiratory complications.

Pulmonary Edema

The occurrence of pulmonary edema (ref. 18) during anesthesia is frequently reported. When it does occur it is usually during inhalation anesthesia. Fisher reports a case of acute pulmonary edema during spinal anesthesia in a patient who had severe circulatory depression and complete respiratory paralysis following administration of 140 mg of 1 per cent metycaine solution. The factors causing the edema were excessive fluids and adrenalin, intravenously, at the time of stagnant circulation.

Backache

Backache occurs in a small percentage of cases. It may be due either to trauma of the soft parts that are traversed by the needle, especially when several attempts to enter the subarachnoid space have been made, or else to a serous meningitis resulting from the wound in the dura and pia; the liberation of a small quantity of blood by penetration of one of the venous plexuses; or the introduction of foreign particles from the needl; or even from the presence of several bubbles of air. No matter what the cause may be, the backache is short in duration and is frequently relieved by placing a pillow under the small of the back. The backache resulting from the induction of anesthesia must not be con-

fused with that following the dorsal recumbent position on an operating table not fitted to conform to the curve of the spinal column. The former quite accurately can be localized to the site of the puncture; whereas the latter is a more diffuse ache. The only treatment necessary is a coal tar derivitive and application of some form of heat therapy (i.e. local wet dressing, diathermy, infra-red lamp, etc.)

Gastric Dilatation and Ileus

This is even less of a factor with spinal than with the inhalation form of anesthesia. There is increased tone of the gastrointestinal tract due to release of sympathetic stimulation and so increased vagal effect. Subarachnoid block acts as a prophylactic measure rather than a caustive factor in post-operative gastric dilatation and ileus. If it does occur it can usually be attributed to rough surgical manipulation.

Late Spinal Complications

Mainly, in this group can be listed the various neurologically manifested symptoms and signs: paresis or weakness of lower extremities; neuritues (radiculitis); paralysis (abducens nerve palsy—ref. 23); myelitis; parasthesias; meningismus; meningitis; encephalitis; anal and vesical incontinence trophoneurotic disorders ranging from decubitus ulcers to a well marked paraplegia; permanent sensory loss; injury to intervertebral disks (ref. 24), arachnoiditis; (ref. 25), and so on. Psychic disturbances can also be included.

It is not within the scope or purpose of this paper to go into detail concerning these subjects. They are fortunately of very rare occurrence and modern technique and precautionary measures have almost nullified them as factors. Many of them are post-operative rather than post-anesthetic complications.

Barrie's (ref. 26) work will be mentioned to further stress how minutely detailed must be the care in technique in order to prevent serious complications. In July, August and September of 1940, eleven cases of meningitis occurred among the 96 patients who were operated on under spinal anesthesia in one theater of the Royal Hospital, Sheffield. During that period the clinical signs and pathological findings resembled each other. One case was fatal and an autopsy obtained. The agent used was from different batches of light procaine.

A review of the circumstantial evidence pointed to a cold filter as being a possible source of infection. This filter was a Berkefeld multiple candle type and was connected directly to the roof water tanks. The outflow water, assumed to be sterile, was used to rinse the lumbar puncture needles which were kept in formaldehype vapor. In view of these findings the case of the filter was promptly discontinued after which no further cases of meningitis occurred. Although circumstantial evidence strongly suggests the contaminated water as a source of infection, direct proof of this has not been obtained.

Summary and Conclusion

Complications of spinal anesthesia are presented. It is our purpose to indicate that in most cases this method of anesthesia was only one of the many contributing factors in causing the complication; a small one at that in many instances. Many of the signs and symptoms formerly considered as complications can actually be labelled as physiological phenomena if properly controlled (i.e., slight headache, slight backache, neuritis.) The well trained physician anesthestologists who have come to the fore in the last decade with their knowledge of physio-pharmacodynamics and refinements and perfection of anesthetic technique have eliminated much of the fear and reproach which formerly enshrouded the method.

All this has helped in rightly elevating spinal anesthesia as a standard method of procedure in our army and cilivian installations. During the time of emergency when it was imperative that we make use of every advantage, we realized that the spinal method had many. Included in its advantages over other methods (especially in our military hospitals) are that the period of hospitalization is reduced and less nursing attention is required (ref. 27), period of convalescence is shorter (ref. 28), the laryngeal reflex is preserved, muscular relaxation is good (ref. 29), and there is an economy of personnel, time and money.

Due to the adoption of the spinal method of anesthesia on a large scale during the war, we were more adequately able to care for our sick and wounded.

BIBLIOGRAPHY

1. Houghton, J. W.: Spinal Analgesia and Sierra Leone, J. Roy. Army M. Corps 13:384-389, 1909.

2. Bainbridge, W. S.: Report on Medical and Surgical Developments Of The War, Washington, D. C. Government Printing Office, 1919.

3. Johnson, L. W.: Medical And Sanitary Care Of The Civilian Population Necessitated by Attacks from Hostile Aircraft, Mil. Surgeon 88:1-24 (Jan.) 1941.

4. Parker, H. L.: Headache Following Diagnostic Spinal Puncture, Proc. Staff Meet., Mayo Clin. (supp. 1) 4:369, 1929.

5. Maxson, L. H.: Spinal Anesthesia (a) p. 258 (b) p. 259, (c) p. 263.

6. Papper, E. M.: Bradley, S. E. and Rovenstine, E. A.: Circulatory Adjustments During High Spinal Anesthia, J.A.M.A. 121:27-32 (Jan. 2) 1943.

7. Koster, H. and Kasman, L.: Spinal Anesthesia, for the Head, Neck and Thorax: Its Relation to Respiratory Paralysis (a) p. 10, (b) pp. 5-6; (c) p. 10.

8. Burnstein, C. L. and Rovenstine, E. A. Circulatory Disturbances Reflexly Inaugurated by Stimulation of the Celiac Plexis. Arch. Surg. 35, 599-602 Sept. 1937.

9. Rovenstine, E. A. and Hershenson, B. B. Anesthetic Complications from Reflexes Excited during Abdominal Surgery, J. Can. Med. Assn., 39, 538, 1938.

10. Rovenstine, E. A. and Martin, Stevens J. Cardio-Vascular Equillibrium During Anesthesia—J. Indiana State Med. Assn.—Vol. 34 No. 4 p. 201-207 April 1941.

11. Best and Taylor—Physiol. Basis of Med. Pract.—3 ed. Chapt. XLIII—p. 798.

12. Sellman, Priscilla—Nausea and Vomiting During Spinal Anesthesia Especially as Influenced by Preoperative Narcotics. J. Anesthes. Vol. 2 No. 3 p. 333-338 May 1941.

13. Harrison, P. W.: Postanesthetic Headache, Arch. Surg. 32:99 (Jan.) 1936.

14. Babcock, W. W.: Spinal Anesthesia in Fact and Fancy, Surg. Gynec. & Obst. 59:94, 1934.

15. Silva, C.—Arch. Med.—Brazil—1:47, 1925.

16. Koster, Harry, and Kasman, L.P. and Shapiro, A. Headache After Spinal Anesthesia. Arch. Surg. Vol. 35, p. 148-154 July 1937.

17. McLaughlin Jr. C. W.,—Brown, John R. Post-Operative Urinary Retention—U. S. Nov. Med. Bull. Vol. XLII No. 5 p. 1025 to 1032 May 1944.

18. Brace, D. E.—J. Anest.—Vol. 3 No. 2 p. 131-139 March 1942.

19. Schotzz, S.—The Clinical Aspects of Pulmonary Atelectasis—J. Anesth.—Vol. 4 No. 3—p. 293-300. May 1943.

20. Lyford, John—Preoperative and Postoperative Infections Of the respiratory Tract in Relation to Inhalation and Spinal Anesthea.—Arch. Surg. (a) Vol. 44 p. 35-40 Jan. 1942. (b) Vol. 44 p. 41-43.

21. Fisher, A. J.: Pulmonary Edema as a Complication of Spinal Anesthesia—J. Anesth. (Current Comment and Case Reports) Vol. 4, No. 6 p. 640-641, Nov. 1943.

22. Hayman, I. R.: Wood, P. M. Abducens Nerve (VI) Paralysis Following Spinal Anesthesia.

23. Munro, D. and Harding, W. G. 2nd.: Lumbar Puncture—Its Potential Role in the Production Of Injuries to the Interverterbral Disk. J.A.M.A. 119:482-483 (June 6) 1942.

24. Haynes, W. G. and Smith F. Cervical Arachnoiditis Occurring After Spinal Anesthesia. J. Anesth. Vol. 3 No. 4 (July) 1942.

25. Barrie, H. J.: Meningitis Following Spinal Anesthesia. Lancet 2:242-243 (Feb. 22) 1941.

26. Troutt, J. M.: Spinal Anesthesia in the Army, Mil. Surg. 66:535-538 (April) 1930.

27. Davis, J. W.: Spinal Anesthesia in Military Surgery, Mil. Surg. 67:46-48 (July) 1930.

28. Donaghy, G. E.: Modern Anesthesia for War Surgery, Mil. Surg. 86:577-581 (June) 1940.

ODE TO A SPECIALIST

(God Bless 'Em!)

A Specialist is a doctor
Who lives his life wth ease;
He trains and studies for many years
To recognize one type of disease.

He knows but one set of symptoms,
Is concerned with nothing but that.
If a patient walks in with a different disease...
The guy's at a loss — he's left flat!

A neurologist, attending a banquet,
Sees a man fall on his skull;
He deftly sticks him with a pin
And inquires if it's sharp or dull?

A psychiatrist walking down the street,
Approaches two fellows with broken necks.
After deliberating for an hour or two,
He attributes the condition solely to sex.

The Obstetrician hears an awful crash—
In the wreck lies a man with broken bones.
He skillfully adjusts his stethoscope
Starts listening for fetal heart tones.

A radial artery is cut on some glass,
From which gushes the fluid of life;
A budding young surgeon arrives at the scene
But the work he does is done with a knife.

Such is the way of the specialist—
A man with a one-track mind.
And any time he steps from his field
He knows not his fore from his hind.

There are many specialists I must omit,
It's impossible to tell of them all.
Have pity on the General Practitioner,
Upon whom all types of cases do fall.

FERRITIN AND IRON METABOLISM

HARRIET WEINSTEIN, S.B.*

IN 1937 Laufberger discovered a protein in horse spleen, stable at pH 4 to 10 and containing approximately 20% iron, which he called ferritin.

Ferritin is not an artifact, as it is possible to obtain crystals of ferritin directly by treating a piece of teased horse spleen or spleen juice with cadmium sulphate (1, 9). According to the Tiselius electrophoretic method ferritin is homogenous, but it is inhomogenous in the ultracentrifuge. Solubility studies and variation in the iron and phosphorous content also indicate that ferritin is not homogenous (1).

These discrepancies have been clarified by the discovery that ferritin is not a definite molecular entity, but consists of a complex of apoferritin-iron hydroxide and about 25% free apoferritin. The mass of these complex particles is not uniform, but apoferritin is a very homogenous protein with a sedimentation constant of S^{o}_{20} 17.6 Svedberg units (11).

When a 3% solution is heated to sixty degrees a coagulum forms which redissolves on cooling. If a similar solution is heated to higher temperatures a coagulum having the appearance of an irreversibly denatured protein forms. Crystals of ferritin are optically isotropic usually with slightly curved edges. The smaller ones are well-formed octahedra; the larger are twinned octhedra formed on the plan of a cube on each face of which is set a tetrahedral pyramid. The crystals are soft and easily crushed under a cover slip but split into distinct fragments rather than smearing into a gel. (1).

As mentioneed above ferritin is not a homogenous protein. When the iron is removed a homogenous protein known as apoferritin is formed. The iron can be removed in the following manner. When the iron of ferritin is reduced from the ferric to the ferrous state in a solution not acid enough to denature the protein (below pH4) yet acid enough to be compatible with the existence of ferrous ions in solution, the ferrous iron can be combined either with O-phenanthroline or with a.a' bipyridine to form a tightly bound water soluble and dialyzable ferrous complex. An iron free colorless protein solution results from which the protein apoferritin crystallizes in the presence of cadmium sulphate. Its crystals are identical with those of ferritin. Ferritin can be regenerated by mixing apoferritin with the brown mother liquor remaining after crystallization. This mother liquor contains iron in a colloidal state not yet fully characterized. No other iron compound was found which was able to combine with apoferritin to form ferritin. It is suggested that the iron of ferritin is in the form of ferric hydroxide micelles dispersed in the interstices of the apoferritin structure (2).

The iron of ferritin is in the rarely occurring three odd electron state. This property is inherent even in the amorphous ferric hydroxide prepared from ferritin by precipitation with alkali; and its magnetic properties are known (3).

Ferritin has been isolated from several species. These, in the order of decreasing content are: horse, human, dog, guinea pig, mouse, rat, pig, rabbit and cat. The organs from which it has been isolated, also listed in the order of decreasing content are: spleen, liver, bone marrow, kidney and testicle. There is a wide individual range in the ferritin content of an organ of a given species.

An antibody against spleen apoferritin has been produced in the rabbit. With the precipitin reaction it is possible to demonstrate that protein crystals of ferritin obtained from one organ are immunologically identical with ferritin crystals from another organ. The precipitin reaction has been used as a sensitive test for the detection of apoferritin in the spleen, bone marrow, liver, testicl, kidney, adrenals, pancreas, ovary and lymph node of the horse. No apoferritin was detected in blood, striated muscle, pituitary or stomach mucosa (4).

The high iron content of ferritin suggests that it may have a storage function. In one study (4) the fate of radioactive iron, Fe-59 injected intravenously in the form of ferric ammonium citrate and in the form of the heme of the red blood cells was followed in dogs. It was found that iron given intravenously as ferric ammonium citrate

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is readily stored in the ferritin of the liver. Iron derived from the hemoglobin of circulating red blood cells after destruction of the cells by acetylphenylhydrazine is in part, at least, converted to ferritin iron in the liver and spleen. This evidence led to the conclusion that ferritin is used for the storage of iron.

Ferritin may take up large amounts of radioactive iron when mixed with radioactive ferric ammonium citrate. Incubation of a guinea pig liver brei with apoferritin and radioactive ferric ammonium citrate and subsequent isolation of the crystalline ferritin and determination of the radioactivity indicates that ferritin is the result of metabolic synthesis which may be the result of a specific enzyme (7).

The mechanism for regulation of iron absorption is localized in the gastrointestinal mucosa (12) and iron once absorbed or administered parenterally is to a large extent, retained. Hahn et al (12) showed that chronically anemic dogs absorb iron at a rate five to fifteen times the normal rate showing that iron absorption is inhibied in the normal animal. Sudden severe bleeding of normal dogs does not bring about an immediate increase in iron absorption but, after several days the absorption gradually increases suggesting that the resistance to iron absorption is related to the iron reserves of the body. After administration of iron the degree of resistance to further iron absorption increases rapidly for several hours. This resistance or mucosal block does not disappear immediately but remains for several days and then gradually declines. The mucosal block might be due to a temporary storage of iron in mucosal cells, perhaps in the form of ferritin. Only when this storage iron in the mucosa has been depleted below a certain level will more iron be absorbed (8).

The demonstration that ferritin is an important factor in the regulation of iron absorption must rest on the following evidence:

1) that ferritin is present in the intestinal mucosa
2) that feeding of iron will result in a rapid increase in the ferritin content of the mucosa parallel to the rapid development of the mucosal block, and
3) that ferritin remains in the mucosa for several days and only slowly disappears in a mucosal block.

Hahn and collaborators developed a semi-quantitative method permitting the estimation of the ferritin content of 2-5 cm. segments of gastrointestinal mucosa of the guinea pig. When ferrous iron is fed, ferritin increases markedly especially in the duodenal and jejunal regions. An appreciable increase is shown in 4-5 hours and a maximal response seven hours after the feeding. After a period of 3-6 days the ferritin has returned to the level of the controls. These data considered together with those obtained in the radioactive iron absorption studies, suggest that ferritin in the mucosa is concerned with the regulation of iron absorption and represents the primary factor for the mucosal block. The feeding of iron leads to an increase in the concentration of the specific protein, apoferritin, which appears in the form of ferritin (8).

BIBIOGRAPHY

1. Granick, S. Ferritin I. Physical and Chemical properties of Horse Spleen Ferritin. Jour. Biol. Chem. *146* 451 (1942).
2. Granick, S. and Michaelis, L. Ferritin II. Apoferritin of horse spleen. Jour. Biol. Chem. *147* 91 (1943).
3. Michaelis, L., Coryell, C. and Granick, S. Ferritin III. The magnetic properties of ferritin and some other colloidal ferric compounds. Jour. Biol. Chem. *148* 463 (1943).
4. Granick, S. Ferritin IV. Occurrence and immunological properties of ferritin. Jour. Biol. Chem. *149* 157 (1943).
5. Fankuchen, I. Ferritin V. X-Ray diffraction data on ferritin and apoferritin. Jour. Biol. Chem. *150* 57 (1943).
6. Hahn, P., Granick, S., Bale. W. and Michaelis, L. Ferritin VVI. Conversion of inorganic and hemoglobin iron into ferritin in the animal body. Storage function of ferritin iron as shown by radioactive and magnetic measurements. Jour. Biol. Chem. *150* 407 (1943).
7. Granick, S. and Hahn, P. Ferritin VIII. The speed of uptake of iron by the liver and its conversion to ferritin iron. Jour. Biol. Chem. *155* 661 (1944).
8. Granick, S. Ferritin IX. Increase of the protein apoferritin in the gastrointestinal mucosa as a direct response to iron feeding. The function of ferritin in the regulation of iron absorption. Jour. Biol. Chem. *164* 737 (1946).
9. Granick, S. and Michaelis, L. Ferritin and apoferritin Science *95* 439 (1942).
10. Nutrition Reviews *5* 45 (February 1947). Ferritin and the absorption of iron.
11. Rothen, A. Ferritin and apoferritin in the ultracentrifuge. Studies on the relationship of ferritin and apoferritin; precision measurements of the rates of sedimentation of ferritin and apoferritin. Jour. Biol. Chem. *152* 679 (1944).
12. Hahn, P., Bale, W., Ross J., Balfour, W., and Whipple, G. Radioactive iron absorption by the gastrointestinal tract. Jour. Exp. Med. *78* 169 (1943).

VISION THROUGH KERATOPLASTY

ERWIN H. ROCKOWITZ

TO TURN back the forever advancing pages of time, one would introduce the very beginning of ophthalmology with the ancient Greek, Roman and Arabian surgeons who operated on cataracts. Their operation was crude, as should be expected; but nevertheless it was a basis for the later study of the surgical therapy of cataracts. The operation consisted of perforating the eye with a needle and pushing the clouded lens backward out of the line of vision; this was termed "couching." The mortality of such an operation was about twenty percent.

In 1748, Daviel performed the first modern cataract operation, consisting of a corneal incision and extraction of the clouded lens through the pupil. Of 434 extractions, only 50 failed. Even though Daviel's operation was a step forward, it was not immediately accepted and couching continued for a long time.

It was not until the latter half of the eighteenth century that the mighty charlatans who attempted to treat eye disease were dethroneed. A professorship in ophthalmology was created for George Joseph Bier of Vienna in 1812, the first of its kind. With this as a nucleus, ophthalmology crystallized throughout the world, and stepped into its rightful place in the organization of medical practice.

It is more than appropriate to review the birth and consequent growth of corneal transplantation. The first to attempt an actual optic graft was Reisinger, but it was his friend and teacher, Himler, who suggested this to him in 1813. Experiments were performed upon the eyes of rabbits with the application of a total graft. Because of lack of success, Reisinger brought his research to an end, as did Desmarres, who met a similar fate. However, Von Hippel, using rabbits' eyes, found that a total graft would become opaque in two or three weeks, so took the initiative to perform a partial graft and found that this would remain transparent for a much longer time.

In 1905, Zirm modified the operation by his use of a graft from a human cornea. Zirm claimed that the following procedures were essential in an operation of this sort: deep anesthesia, the avoidance of antiseptics, the protection of the graft between two pieces of gauze moistened with sterile physiological saline solution, and finally keeping it warm in steam until it could be placed in position.

Opacities of the cornea can result from inflammation, ulceration or injury. The cornea may become faint and cloud-like, the condition called nebula. When this becomes more pronounced, it is termed macula, and a dense white cornea is a leucoma. Such pathology of the cornea simulates a windowshade with the consequent partial or total loss of vision. When the cornea is involved to such an extent that sight is nearly totally inhibited, corneal grafting has proved to be a practical operation. Dr. P. Castroviejo states that in favorable cases the average vision obtained is 20/50 and it is not infrequent to obtain vision of 20/20. The opacities of the cornea interfere with proper vision when there is an encroachment upon the pupillary area of the cornea. The degree of effect depends upon the amount of opacity.

Ideal results from corneal transplantation have been obtained in cases with normal anterior chambers. Experiments have shown that transplants taken from animal corneas never remain clear. Also, the transplants are less likely to remain transparent when the host cornea is covered by pannus.

There are two types of corneal grafting: tectonic and optic. The former is the budding in or up of new corneal material to replace what was lost. The tectonic type of graft is for pathologic corneas which are due to a neoplasm removal or a hypertrophied bulbar conjunctiva and subconjunctiva. The optic type is most usually employed for a blinding total leucoma.

All of the successful corneal transplants performed at the Oddessa Eye Clinic in Russia were on those corneas which contained some transparent elements.

The ramifications of keratoplasty have been greatly enhanced because of the sight-giving engineering of Filatov. Filatov presented the possibility of utilizing the cadaver's eye for corneal transplants. He claimed that it is essential to keep the cornea within a balanced temperature, not above 4 to 6° centigrade. The cornea of a cadaver's eye, enucleated forty-one hours after death and kept in an ice chest at 4°C. for a few hours, was employed. At the time of operation, the cornea to be used was slightly opaque

over the whole surface. An individual operated upon had been blind for eighteen years because of a varicella infection and the right eye had both nystagmus and a dense leukoma; however, light projection was fairly good. The outcome of this keratoplasty took well and the transplant remained transparent throughout a fourteen month period of observation. Filatov greatly stressed the optimistic outlook of the cadaver's eye as a source of a corneal graft. Other materials used for transplants are eyes of living human beings who have had their eye enucleated because of serious ailments.

Filatov has carried out transplantations in the following ways: (1) total corneal transplantation; (2) part of its layers; (3) a partial penetrating transplantation of the cornea. Of the three types, the latter has been found by Filatov to be the most successful; therefore, the description of this operation in some detail follows.

Before the operative field is isolated, one percent brilliant green is applied to the skin of the face and eyelids; this is for disinfecting purposes. Akinesia is obtained and both epibulbar and retrobulbar anesthesia is used. The conjunctival sac is washed with brilliant green. The superior and inferior recti muscles are stibilized with a bridle suture; restless patients require sutures on all of the recti muscles.

In the fixation of the transplant—the second stage of the operation—Filatov used two methods. In one case, an egg membrane covers it, or else he applies a covering conjunctival flap. Dr. R. T. Paton claims conjunctival flaps should be discouraged, as they lead to complications. With the former, an Elschnig's suture is drawn through the conjunctiva at the upper end of the leukoma and passed with two needles at the lower end of the leukoma; similarly, a suture is drawn in the horizontal medium. With the conjunctival flap, the flap of the sclera conjunctiva is cut at the upper part of the eye. This flap begins at the superior rectus muscle and the base is at the limbus; the flap is six millimeters wide. Two sutures with double needles are pulled through the lower end of the flap and through the conjunctiva at the limbus; they are temporarily turned up. The upper defect of the conjunctiva is left unsutured.

The third stage of the operation requires excision of the corneal transplant. This involves washing the eye with a solution of the brilliant green, wrapping it in dry gauze and holding it firmly with the left hand. The trephining is done with a Von Hippel's trephine, four millimeters in diameter. The eye is emptied of its contents; the sclera, pressed against the posterior surface of the cornea, serves as a supporting base for the trephine. A prophylactic spatula is used for the prevention of both injury of the lens and loss of vitreous as there can be a loss of vitreous if there is a lens injury when the trephine is used. This prophylactic spatula is placed through the anterior chamber. To carry out this procedure; first, two incisions are made by means of a Von Graefe's knife, the internal incision being three millimeters and the external six millimeters wide. Next, the ivory spatula, five and one-half millimeters wide is inserted through the incisions, with sutures pulled through the holes at the ends of the spatula.

Trephining the leukoma is stage five of the operation; and stipulates cutting the disk of the leukoma with the spring-controlled trephine. The crown of this trephine has a diameter of 4.05 mm. (the transplant material being 4.0 mm. in diameter); thus, great accuracy and precision is required for this procedure.

The next step is the placing of the transplant and its fixation. The transplant is placed in the opening which is closed posteriorly by the spatula. The conjunctival flap with its epithelial surface is stretched over the transplant and the sutures tied with three plain knots. Radial incisions are made on its surface for better fitting. Elschnig's crossed sutures are drawn over it and tied.

The removal of the spatula is the final step. After placing the transplant and covering it well, the spatula is removed from the anterior chamber by its external end with a sure, quick movement. The bridle sutures are removed and atropine and a binocular dressing is applied.

The vast progress made in ophthalmology in the past century is an incentive and a hope to offer a new colorful life to the sightless. To carry out research on a sight-giving basis is truly an optimistic and heart-warming call.

BIBLIOGRAPHY

1. *A Hundred Years of Medicine*, C. D. Haagenson, and W. E. B. Lloyd.
2. *Diseases of the Eye*, May.
3. *Ophthalmic Surgery*, Beard, 1914.
4. *Archives of Ophthalmology*, 170:13 (1935); 271:13 (1935); 321:13 (1935); 83:33 (1945).

THE PRODUCTION OF CREATINE-CREATININE DESTROYING ENZYMES FROM HUMAN URINE AND GASTRIC JUICE

HOWARD H. BEARD, Ph.D.*

IN OUR last studies on this subject creatine-creatinine destroying bacteria were cultivated from rat feces and urine (1, 2). In our search for other sources of these enzymes we have used human urine and gastric juice. The enzymes produced increase their ability to destroy creatine and creatinine with increasing concentration of the bacteria in the solution being tested. Glycocyamine, glycocyamidine, hydantoic acid and hydantoin were not destroyed. This made possible the use of these enzyme suspensions in studying the metabolism of these substances and in invetigating the nature of the residual Jaffe material in beef liver.

Experimental

Human urine was collected in a beaker and allowed to stand at room temperature for several days. The organisms, which collected on top of the urine and on the sides and bottom of the beaker, were separated from the urine and worked up by our former technique (2). The sample of gastric juice was allowed to stand at room temperature and treated likewise.

The bacteria from these two batches were placed in separate 500 cc Erlenmeyer flasks and covered with 100 cc of Chicago tap water.* Into each flask was placed 10 mg. of NaCl and 6 gamma of biotin. The flasks were stoppered with cotton and incubated at 37°C for various lengths of time. The complete disappearance of creatine or creatinine was followed by the use of alkaline picrate before and after heating the sample with HCl. The Cenco-Sheard photolometer was used for estimation of color intensities and the Coleman pH electrometer for determinations of pH The bacteria were then collected by centrifuging and the whole was placed in the second flask containing fresh amounts of ingredients, etc. In this way increasing amounts of the bacteria were present in each succeeding run.

Results

Exp. 1. The enzyme destroyed from 1.1 to 13 mg. creatinine and from 3.1 to 10 mg. creatine per hour, from the first through the fourth and fifth runs.

Exp. 2. The odor of ammonia was always produced and the pH usually increased from 7 to 8.8. After removing the bacteria at the end of the fifth run the clear solution gave a heavy precipitate with xanthydrol indicating the presence of urea.

Exp. 3. 200 mg. of urea with NaCl and biotin in Chicago tap water were incubated with the creatinine enzyme with the odor of ammonia given off in every instance. This is further proof that the enzyme converts urea into ammonia.

Exp. 4. 100 mg. each of glycocyamine, glycocyamidine, hydantoic acid, and hydantoin, in separate flasks incubated with the creatinine enzyme under the above conditions, showed no change in color produced with alkaline picrate in the photolometer. Proper precautions were observed in these cases to obtain the maximum color development in control and experimental flasks.

Exp. 5. The bacteria produced from human gastric juice standing in air at a pH of 7.1 were incubated with the creatinine-salt-biotin solution. Results are presented in Table 3. The enzyme destroyed creatinine from 0.7 to 2.7 mg. per hour with ammonia production and a final pH of about 8.8.

Exp. 6. The optimum pH for enzyme action in the destruction of creatinine ranges from 7 to 10.*

* Dept. of Biochemistry, The Chicago Medical School.

*The composition of Chicago tap water in parts per million was as follows: turbidity 1, color 3, total residue, 157, dissolved solids 114, silica 3.1, Al and Fe oxides, 1.3; Ca, 32.2 Mg, 10.3, Na 2.2, K, 1, SO, 14, Cl 4.6, CO_3 69, alkalinity (phenolphthalein) 2, (methyl orange) 115, raw water pH 8.1, total hardness (calc. as $CaCO_3$) 122, Free NH_3 0.04, albuminoid N, 0.004, organic N, 0.0018, nitrate N, 0.2, oxygen consumption (30 min) 2.5. (Report from the Chicago Purification Division, 9-28-46).

Since this study was completed further work on the identification, isolation and properties of the enzyme have been completed and will be published later (Cf Kopper and Beard, Federation Proc., 6, Part II, 267, 1947).

Summary

When human urine is allowed to stand at room temperature for a few days bacteria are produced on top of the urine and on the sides and bottom of the beaker. After separation from the urine and incubation with creatine and creatinine these substances were destroyed from 1 to 13 mg. per hour from the first through the fifth runs. The enzyme secured from human gastric juice destroyed from 0.7 to 2.7 mg. creatinine per hour.

The uptimum pH for enzyme action was from 7 to 10. The pH of the different solutions increased from 7 to about 8.8. Ammonia was produced and the solution remaining after the removal of creatinine gave a heavy precipitate with xanthydrol for urea. The creatinine enzyme transforms some urea into ammonia.

The creatinine enzymes above did not destroy glycocyamine, glycocyamidine, hydantoic acid nor hydantoin.

No creatinine enzymes were produced from the following: E. coli, staph albus, canned tomato and pineapp'e juice, fruit cocktail or bread mold.

LITERATURE CITED

1. Beard, H. H. Arch. Biochem., 2, 363, 1943.
2. Beard, H. H. Arch. Biochem., 5, 293, 1944.

RUTIN — A DISCUSSION

ARMENTANO and his associates in 1936 prepared an extract of lemon peal which reduced capillary fragility and decreased capillary permeability. The principle was different from ascorbic acid and was able to improve certain hemorrhagic conditions resistant to the latter. The new vitamin was called Vitamin P and, later Citrin. Subsequent studies suggested that the active principle of the lemon peel extract was hesperidin, a substance very similar, if not identical with rutin. Rutin is a flavone glucoside found in many plants, including tobacco, buckwheat, forsythia, hydrangea and others. It was first isolated from tobacco leaves in 1860 and received its first clinical trial in 1944 by Griffith and his associates. With the perfecting of the methods of extraction from buckwheat, rutin has become more generally available and much cheaper. Griffith and associates reported the results of a study of 1219 patients with various hemorrhagic disturbances. Of these, 255 had increased capillary fragility and were treated with rutin. In 152 cases, or 88%, the capillary fragility returned permanently to normal, in 12% the results were temporary or negative. More recently Shanno studied the use of the drug in a variety of conditions associated with increased capillary fragility, including 24 cases of hypertension. Some of these patients had been treated with thiocyanate and had increased capillary fragility. Many were benefited by the use of rutin. In 1946 Griffith and associates reported on an investigation of 1600 hypertensive patients. Of these, 18% had increased capillary fragility and were more likely to be subject to hemorrhagic complications, such as apoplexy and retinitis. The administration of rutin reduced the capillary fragility to normal in the majority of cases.

Rutin seems to be of value in the treatment of retinal hemorrhages and retinal vascular occlusion as a result of thrombosis. In the latter instance it has been used in association with dicumarol (MacLean and Brambel). Kushlan obtained favorable results in a case of hereditary hemorrhagic telangiectasis; Hanum in the treatment of hemorrhagic diabetic retinitis and in increasing the permeability of the blood-aquaeus barrier thus reducing the intraocular pressure in glaucoma. Should these early reports be confirmed, rutin may prove to be of great value in the treatment of increased capillary fragility occurring in many diseases, such as hypertension, diabetes, apoplexy, hereditary hemorrhagic disorders, purpuras due to drug intoxication, purpura neonatorum and others. Recently, Raiman and associates demonstrated that rutin protects the guinea pig from the effects of horse serum anaphylaxis, but not from the effects of histamine shock. The interpretation of these results is not clear, but it may indicate another interesting therapeutic application of rutin.

To avoid disappointing results Rutin should be used only in cases in which the capillary fragility is abnormally high. This can be determined by counting the number of petechiae produced in a limited area of the forearm by the application

(Continued on page 21)

Abstracts

HEPARIN THERAPY IN ACUTE DEEP VENOUS THROMBOSIS. Gunnar Bauer, J. Amer. Med. Asso., 131:196, May 1946.

In the summer of 1940 at the Mariestad Hospital, Sweden, a method was introduced for treating thrombosis of the deep veins of the leg, the main principles of which were: (1) early diagnosis; (2) intensive heparin treatment; and (3) early mobilization.

Until 1936, the phlebothrombotic process was universally considered to commence in the femoral or pelvic veins. Not until phlebography had been taken into us was it possible to carry on research and make studies of what actually occurred.

The whole process begins with thrombus which arises in a muscle vein and projects into the lumen of one of the large venous trunks of the lower part of the leg. Here it becomes the starting point of deposition thrombus which continues growing upward in the direction of the blood stream. The next stage is the gradual obliteration of the larger vessels with the development of freely waving eel-like thrombotic formations up to 40 to 50 cm. in length. The wall of the vein is as yet not involved in any way, and the thrombus is anchored only at its lowermost end far down in the leg.

This condition, which obviously entails a great risk of embolism, does not generally last more than 24 to 48 hours. Within that time a development takes place which may proceed along two different lines. One is that the waving thrombus produces an embolus. By far the commonest development is for the thrombus to continue growing in thickness, block up the lumen of the femoral vein, begin to involve the endothelium and to become attached to the vascular wall along its entire length. A typical phlegmasia alba dolens arises. We thus see that the phlebothrombosis can lead to a thrombophlebitis and produce typical symptoms.

After the deep blood channels in the leg have been destroyed by thrombosis, recanalization of these veins practically never occurs. The drainage of venous blood from the lower part of the leg is taken care of by an accessory system of veins consisting exclusively of subcutaneous veins, usually with the great saphenous vein acting as the chief carrier of the venous return. A mild state of venous stasis is always present, however, causing chronic edema in the lower part part of the leg. As a result of unfavorable emptying conditions and of constant overloading, there arises in the accessory system during the course of the year, a state of degeneration which is manifested in the fact that the superficial veins become distended and tortuous and the valves defective. This degeneration causes nutritional disturbances and leads in time to the appearance of the typical, leathery, indurative lesions on the lower leg and to leg ulcers.

If the thrombosis could be diagonsed in its early stages, the subsequent sequellae of an advanced condition could be prevented. With phlebography, the diagnosis of early thrombosis has been made and the administration of heparin to prevent further formation of the deposition thrombus has been successfully used.

RUTIN—

(Continued from page 20)

of an inflated blood pressure cuff. The technic has been described by Gothlin and the results are expressed as the Gothlin Index. Rutin is usually administered in doses of 2) mg two or three times a day, often in association with 50 mg of ascorbic acid.

BIBLIOGRAPHY

Armentano, L. et al., Deut. Med. Wschr. 1936, *62*, 1325

Griffith, J. Q. et al., Amer. Heart J. 1944, *28*, 758 and Proc. Soc. Exp. Biol. & Med. 1944, *55*, 228.

Shanno, R. L., Amer. J. Med. Sci. 1946, *211*, 539.

Griffith, J. Q. et al., Exhibit at the Scientific Assembly of the A.M.A., San Francisco, July 1946.

MacLean, A. L. and Brambel, C. E., Tr. Am. Ophth. Soc. 82d annual meeting, San Francisco, 1946.

Kushlan, S. D., Gastroenterology 1946, 7, 199 and J.A.M.A. 1947, *133*, 716.

Hanum, S. Acta Ophth., Supp. 16, p. 3, 1939.

Raiman, R. J. et al., Science 1947, *106*, 368.

The Technic of Therapy: Immediately after the diagnosis of thrombosis had been made, 150 mg. of heparin was administered. An interval of four hours elapsed between doses, and the last dose was given late at night. On following days three to four injections were usually given, with early morning and night doses of 150 mg. and a mid-day dose of 100 mg. After a few days the temperature returned to normal and swelling and tenderness decreased. The heparin doses were then decreased to two injections of 100 mg. each, and on the last day an evening dose alone. Complete mobility was allowed. After the acute signs of thrombosis had subsided and the actual heparin therapy terminated, an evening dose of 100 mg. was given each day for one week. After that, one injection every other evening was given and then every third evening. The mortality dropped from a pre-heparin era of 18% to less than 0.1%. The length of stay in bed was reduced from about 40 days to less than 5 days. The chronic incapacitating sequellae usually do not appear.

Complications: The only complications of any kind consisted of a mild hematuria, which was observed in three cases. The condition lasted for only two days at most and was not followed by other signs of renal irritation.

THE USE OF POTASSIUM CHLORIDE IN THE TREATMENT OF THE DEHYDRATION OF DIARRHEA IN INFANTS. C. D. Covan, Jr. & D. C. Darrow, Jour. of Ped., 28:541, May 1946.

For practical purposes no fundamental new principle in the treatment of diarrhea has been introduced in the last 20 years. It was shown by Darrow and his collaborators that the loss of body potassium in a severe diarrhea could reach as much as one-fourth of the total body potassium. It was further demonstrated that this loss of potassium is not accounted for by disintegration of the cells, for the deficit of potassium was not accompanied by a loss of nitrogen and intracellular phosphorus.

During periods of fasting, when all fluids were given parenterally, retention of potassium unaccompained by a positive balance of nitrogen and intracellular phosphorus was produced by the addition of potassium chloride to the solutions in general use for fluid and electrolytic replacement.

The method of treatment as used here is as follows:

(1) Initial treatment of shock: Whole blood or plasma, 10-20 cc. per kg., together with equal volume of physiological saline.

(2) Period of fasting: Oral administration of water and food was withheld until all evidence of dehydration was overcome, nausea was no longer manifest, and intestinal functions had been partially restored. This period lasted from 24 hours to six days.

(3) Replacement of body fluids and electrolytes: Intravenous or subcutaneous fluids, 80-150 cc. per kg. of a mixture of potassium chloride, sodium chloride, and sodium lactate was administered. The rate of injection varied; it was given as rapidly as 2 cc. per minute over a period of 4 hours when necessary. Usually, however, it was given for 8-12 hours by drip method. During this initial period enough 5% glucose solution was injected intravenously to make the total fluid intake equal to 150-280 cc. per kg.

(4) Maintenance of body water and electrolytes: After the first day, smaller amounts of the electrolyte solution were given daily (20-50 cc. per kg.). This was given as long as the stools remained watery. In addition sufficient 5% glucose was added to make the total fluid intake equal to 150-200 cc. per kg.

(5) Vitamins: Upjohn Solu-B was added to the glucose. One cc. of crude liver was injected I.M. two times a week.

(6) Feeding: This is begun when there is no evidence of dehydration or watery stools. Milk with 2% fat, made up of equal parts of full strength powdered whole lactic acid milk and powdered skimmed milk, plus 5% dextri-maltose, was given. During the first day 10 calories per kg. diluted with 150 cc. of fluid per kg. was the amount given. If the infant didn't take it, it was supplemented with I.V. feeding.

By using the control group which received exactly the same treatment but without the potassium chloride, a notable difference in mortality was found. Without the use of potassium the mortality was 33%. With potassium administration, the motality wa sonly 6%, a marked drop.

Complications: The dosage of potassium given was just below that level which could produce heart block if none of the salt was transferred to intercellular tissue or excreted. The level associated with heart block is 10-12 millimols per liter. In all patients but one, the level was far below intoxication level.

In the one patient in which the level was 12.3 mm. per liter, the clinical symptoms of heart block presented themselves. Immediate injections of 15 cc. of 10% calcium gluconate and 150 cc. of 17% glucose improved the child. It has been found that severe dehydration causes a relative high concentration of potassium and the shock causes potassium retention. It is therefore necessary to treat shock and circulatory collapse first, before starting potassium therapy.

The following are the continuation of abstracts of lectures given at the Annual Clinical Conference of the Chicago Medical Society on March 4-7, 1947.

* * * *

PSYCHOSOMATIC GYNECOLOGY. Dr. J. P. Pratt, Head of the Dept. of Obstetrics and Gynecology, Henry Ford Hospital, Detroit.

THE EMOTIONAL and visceral stability of the human are very closely related psysiologically, and repeated trauma in one direction may result in a symptom complex of the other.

There are six common fears allied with gynecological operations:

1. Death—more than 50% have this fear and the answer is to assure the patient by statistical knowledge.
2. Permanent crippling effects.
3. Loss of libido.
4. Assumption of masculine traits.
5. Fear of getting older.
6. Fear of divulging secrets under anaesthesia.

To circumvent these fears the patient should be assured thoroughly before all operations.

Furthermore, many gynecological problems which seemingly require medical or surgical intervention, are amenable to the psychotherapeutic removal of a fear or an anxiety. Dysmenorrhea can commonly be traced to a fear of pregnancy, and disorders such as amenorrhea, dyspareunia, frigidity, and similar conditions can likewise be traced, for the most part, to fear.

In summary it may be said that simple fears can be useful, but prolonged fears may prove dangerous and therapy by simple logic is advisable.

THE GERIATRIC PATIENT. Dr. Edward L. Bortz, Associate Professor of Medicine,, Graduate School of Medicine, University of Pennsylvania, Philadelphia, Pa.

Whereas the average life expectancy of 75% of all newborns reached only twenty-five years in nineteen hundred, today that life expectancy is fifty-seven years—and the average life span exceeds sixty-five years. This longer life is due to our high standard of living and our continued and successful campaign against disease.

As a result of this campaign, the common disorders of later years are mostly degenerative in origin, and not infectious as once was the case. The disorders fall primarily in the following categories:

1. Cardiovascular
   a. Arteriosclerosis
   b. Hypertension
2. Nephritis
3. Diabetes
5. Arthritis
4. Cancer
6. Anemias
7. Secondary respiratory infections
8. Mental deterioration

In the older individual the greatest enemies are fatigue and boredom. Fatigue is a major contributing factor to the degenerating processes in the body, and mental fatigue is extremely dangerous. Boredom is the chief cause of mental deterioration, whereas tissue fatigue and nervous exhaustion are the principal causes of coronary occlusion.

In prescribing for vitality in later years, a program should include the following ten basic rules:

1. Proper diet
2. Adequate elimination
3. Rest—in sufficient amounts

4. Purposeful activity
5. Emotional control
6. Sense of humor
7. Contacts with young individuals
8. Intellectual growth
9. Continuous education
10. No retirement

Elderly people should have outlets for their abilities and society should encourage new interests for those who leave work because of their age. Most important, the older patient should feel that his activity is an addition to society—that he is an active participant and not a charge of society.

SURGICAL PROBLEMS IN DIABETES MELLITUS. Dr. Leland S. McKittrick, Associate in Surgery, Harvard Medical School, Boston, Mass.

It has been stated by Joslyn that, eventually, diabetics require surgery. Diabetes itself is not a contra-indication to surgery, however, several pertinent factors need be kept in mind at all times.

Diabetes leaves an injury, thereby handicapping the diabetic patient. The physician should use every available clinical aid in trying to evaluate the damage—especially that done to the cardio-vascular-renal system.

Secondly, the pre- and post-operative care of the patient must be very meticulous. The hospital in which the surgery is performed should have a particular interest in diabetics. The laboratory at this hospital should have the equipment to perform all metabolic tests, and a metabolic specialist should always be on hand.

A third factor to be considered is the anesthesia. Any type may be used in elective cases, but emergencies require the use of an anesthetic without an effect on metabolism. This requires thought and care in selection.

Carbuncles and lower extremity injury with subsequent infection and ulceration present a fourth problem among surgical diabetics. The introduction of penicillin has altered the prognosis of such cases, so that now, with early hospitalization, proper medical care, and penicillin (300,000 to 500,000 units /24 hours), the response is good and rapid—where the course was previously dangerous and long.

VAGOTOMY IN PEPTIC ULCERS. Dr. Lester R. Dragstedt, Professor of Surgery, University of Chicago School of Medicine, Chicago, Illinois.

Vagotomy has proven successful in one hundred and seventy patients with all types of peptic ulcers. Results of the operation depend on resection of the vagal branches to the stomach—thus abolishing the nervous phase of gastric secretion. In peptic ulcer patients the nervous phase of secretion is exaggerated, and in dogs where resection was performed the gastric juice output was observed to be one-fifth to one-sixtieth of the amount originally produced. Unfortunately, peptic ulcers, per se, are a psychosomatic disease, and in ulcer patients hyperacidity occurs when no stimuli exist.

In order to cut the vagus nerves to the stomach the operation must be directed at the esophagus. All fibers of the vagus must be divided, including those of Meissner's Plexus. Vagotomy is done by an eighth rib incision over the pleura and the proximal ends of the nerves are transplanted in the pleural cavity.

To test the completeness of the vagus section, there are two acceptable methods:

1. Hypoglycemia is known to stimulate the vagal center in the brain and thus to stimulate secretion. However, if vagotomy is done completely there will be no secretion.

2. Select food that the patient likes and serve it appetizingly. Instruct the patient to chew but not to swallow. All normal individuals respond to this with secretion, but this is abolished if the vagotomy is done completely.

Vagotomy accomplishes the following:

1. It removes the augmenter influence of gastric motility.

2. There is no disturbance of motility of the esophagus and cardia. Theer may be an increase of the tonus of the pylorus.

3. The effect on gastric sensation is immediate with a complete disappearance of ulcer pain. Relief is exceptionally complete and permanent if resection itself is complete.

4. Benign peptic ulcers will heal as a result of complete section.

Book Review

SYNOPSIS OF OBSTETRICS. J. C. Litzenberg, B.Sc., M.D., F.A.C.S., Professor Emeritus of Obstetrics and Gynecology, University of Minnesota Medical School, Minneapolis. Third Edition, revised with 157 illustrations, including 5 in color. 399 pp. C. V. Mosby Company, St. Louis, 1947.

We usually find fault with synopses because of the inevitable omission of some of the more important fundamentals regarding the subject discussed. It is for this reason that Dr. Litzenberg's digest of didactic and practical obstetrics is so unusual. In 399 pages, a more than adequate synopsis of obstetrical procedures is presented in outline form.

It is evident that limited space necessitated brevity, and omission of less essential details. However, an endeavor was made by the author to place due emphasis upon the really important material. His aim has been to minimize the more or less irrelevant; evaluate the questionable; emphasize the important; and at the same time, to maintain that balance between minimum and maximum stress so necessary to develop sound judgment.

* * * * * *

HANDBOOK OF COMMUNICABLE DISEASES. F. H. Top, A.B., M.D., M.P.H., F.A.C.P. Medical Director, Herman Kiefer Hospital. Clinical Professor of Preventative Medicine and Public Health, Wayne University College of Medicine; Extramural Lecturer in Infectious Diseases and Epidemiology, School of Public Health, University of Michigan; Consultant, Preventative Medicine Section, Surgeon General's Office, U.S.A.; and collaborators. Second Edition, revised with 95 illustration and 13 color plates, 948 pp. C. V. Mosby Company, St. Louis. 1947.

The Handbook of Communicable Diseases is intended as a text or handy reference for all persons whose professional duties necessitate contact with certain communicable diseases or infestations. Dr. Top has attempted to present the material in as concise and yet as thorough a manner as posible. The diseases have been classified by common portal entry and are discussed thoroughly with emphasis on epidemiological and public health aspects of the entities discussed

At present these is a need for such a book. It is simple, yet deals with such important subjects as management, specific prevention and immunity with great clarity and sufficiently thorough to satisfy the requirements of most physicians. The latest modes of therapy are disucssed to great length allowing the reader to judge for himself which therapeutic procedures are most suitable for his particular problem.

* * * * * *

METHODS OF DIAGNOSIS. Logan Clending, M.D., F.A.C.P., Late Professor of Clinical Medicine and History of Medicine, University of Kansas School of Medicine; and E. H. Hashinger, M.D., F.A.C.P., Professor of Clinical Medicine, University of Kansas School of Medicine. First Edition, with 43 illustrations. 840 pp. C. V. Mosby Company, St. Louis, 1947.

"Gentlemen, the cause of Science imposes on you a difficult task. You must not assume that you have the explanation for any phenomenon of nature until every alternate hypothesis has been exhausted." (Claude Bernard). Methods by which a physician obtains a diagnosis are varied in nature, depending on the individual and the logic utilized. The authors of the work on diagnosis stress, throughout, the necessity of the student "to learn to open his eyes and see, and then to shut them and think."

The average textbook in medicines takes up the description of diseases under their proper names and is therefore of little help to the physician at the bedside of his patient until after he has determined what disease is present. This work, therefore, discusses the diagnostic possibilities of a given case—starting from the symptoms, or from the signs, or laboratory data, X-ray film, or the F.K.G. record which the patient presents.

This volume is a thoroughly learned presentation. It is divided into four parts: Principia Diagnostica, The Patient, Anatomic Region, and Laboratory and Special Procedure. It is a most worthy addition to any library.

DIAGNOSTIC BACTERIOLOGY. Isabelle Gilbert Schaub, A.B., and M. Kathleen Foley, A.B. Third Edition, 532 pp. The C. V. Mosby Company, St. Louis, 1947.

This very useful and practical book, as the sub-title explains, is "a textbook for the isolation and identification of pathogenic bacteria for medical bacteriology laboratories."

The text not only consists of the usual methods of identification of the pathogenic microorganisms commonly dealt with, but includes theoretical discussions and explanations which should, indeed, clarify any of the problems with which the laboratory worker is invariably confronted. In addition, there are many useful and informative tables which will enable the worker to make differential diagnoses almost at a glance.

The nomenclature has been revised to conform to the most recent opinions, and all types of new methods and techniques have been incorporated.

The book is divided into three parts: the first deals with bacteriological diagnoses which includes all the procedures for the cultivation of pathogenic bacteria from clinical and autopsy material. Part two deals with serological diagnoses—including the typing of pneumococci (although fast becoming of no practical value except for prognostic value and chemo-sensitive strains), while the third part of the book is concerned with media, sera, staining techniques, reagents, and tests.

The book is so arranged that the even numbered pages are blank for the purpose of making suitable comments or notations when the occasions arise.

Two outstanding features of the book are: (1) a very complete and excellent index, and (2) the manner in which the book is printed. The print has been excellently chosen and the varying sizes of type—including the italics—make it extremely simple and enjoyable to read.

The methods chosen are simple and easily understood and should prove of inestimable value to any student or technician working in the practical—the diagnostic—aspects of bacteriology.

SEMINARS

Schedule of meetings and lectures to be held during the Winter Quarter, 1948, on Wednesday at 1:00 P.M., in Amphitheater A. Students, faculty, and guests are invited:

January 7—Medicine Journal Club: "Recent Advances in Internal Medicine." Dr. Peter Gaberman, Associate Professor of Medicine, The Chicago Medical School.

January 14 — Biochemistry Research Seminar: "The Amino Acid Composition of Proteins." Dr. Leo J. Saidel, Instructor in Biochemistry, The Chicago Medical School.

January 28—"The Metabolism of Foodstuffs in Diabetes." Dr. Samuel Soskin, Medical Director Michael Reese Hospital.

February 4 — Pediatrics Journal Club: "Recent Advances in Pediatrics." Dr. Aaron Grossman, Instructor in Clinical Pediatrics, The Chicago Medical School.

February 11—Pathology Research Seminar: "The Rh Factor—Recent Studies." Dr. Israel Davidsohn, Chairman of the Department of Pathology, The Chicago Medical School.

February 18 — "The Mechanism of Fluoracetic Acid Poisoning." Dr. John O. Hutchens, Chairman of the Department of Physiology and of the Toxicity Laboratory, The University of Chicago.

March 3—"The Technique of Tracer Work." Dr. Enrico Fermi, Professor of Physics, Institute of Nuclear Studies, The University of Chicago.

March 10 — Anatomy Research Seminar: "The Stimulation of the Cerebral Cortex in the Unanesthetized Monkey.' Dr. George Clark, Associate Professor of Neuro-Anatomy, The Chisago Medical School.

March 17 — Obstetrics and Gynecology Journal Club: "A Review of Recent Obstetrical and Gynecological Literature." Dr. Egon W. Fischmann, Chairman of the Department of Obstetrics and Gynecology, The Chicago Medical School.

Social Notes

CASE REPORT

Presenting Complaint:

Bachelors in Medical School decreasing — 2 years.

Present Illness:

Medical Students remained perfectly (?) single until two years ago when it was noticed that a few students developed a glassy far-away look in their eyes. At first this was regarded by the majority of students as a sporadic outbreak, but recently the symptoms have become much more pronounced, and what with the influx into the school of many chronic cases, the picture took epidemic proportions. Patients complained of persistent illusionary images appearing before their eyes that resembled members of the opposite sex These complaints have been progressive until the present time.

Past History:

Jacqueline Yvonne Pich, daughter of Mr. and Mrs. Melvin M. Pich ('51), will celebrate her first birthday on January 14, 1948. In spite of this occurrence, a new outbreak is expected some time in January in the family of Al and Francis Blumenthal ('51). Fran insists that she has definite indications that things are going to start popping very shortly.

Inventory of Symptoms and Findings:

Head—There must be obvious cerebral damage with concomitant euphoria to account for the sudden onset of symptoms in so many cases.

Eyes—It is very easy to see what was the exciting cause for Theodore Cohen ('48) getting married to the former Miss Barbara Zweig on September 21, 1947, in New York City.

Ears—Tinnitus of a bell-like quality accommanied the union of Morris Binder ('48) and the former Miss Helen Bruss at the Bismarck Hotel in Chicago on June 11, 1947.

Nose—Pleasant olfactory sensations resembling well-cooked food have been noted ever since June 1, 1947, by Herbert Lipschultz ('48), at which time the former Miss Jean Tucker started trying to fatten up her brand new husband.

Mouth—Larry Elegant and the former Miss Joan Sherman (Murray's sister) haven't stopped talking about it since December 21, 1947, when this Sophomore entered into some legal contract with Joan.

Neck — Jerome Z. Litt ('50) complains that he can get no further than this with Esther Novet until Easter, when they will be married in Brooklyn.

Heart—The etiology in this case is definitely related to cardiac dilitation and softening. Jack Margolis ('49) almost fibrillated during his engagement to Evelyn Pliskin of New York City on December 25, 1947.

Gastro-intestinal — Melvin Leichtling ('48) reports that since his engagement to that cute little brunette, Miss Elayne Rosen of Chicago, on September 1, 1947, his appetite for her has increased so greatly that he will make her a Leichtling in June.

Genito-urinary — Physiological for this condition.

Reflexes—Mutual conditioned reflexes have developed between Caroline (Belle of the Senior Class) Winograd and classmate Harold Brown to such an extent that it was officially announced on November 15, 1947, that they would remain together after graduation, and foster the reflex indefinitely as of June 20, 1948.

Laboratory Reports:

Joe Kahn ('51) and the former Miss Phyllis Silberman reported that successful tolerance tests mutually conducted since December 21, 1947, have definitely proved that marriage confers a lasting immunity to the syndrome of Single Existence.

Summary:

Finding definitely indicate the epidemic and even pandemic proportions of this outbreak.

Diagnosis:

Marriageitis.

Treatment:

Symptomatic.

Prognosis:

Hopeless! Sooner or later almost every Medical Student will succumb.

School And Faculty Notes

The Mount Sinai Hospital of Chicago has entered into an academic affiliation with The Chicago Medical School for the purpose of teaching students in the third and fourth years. This affiliation became effective as of the academic year 1947-48 and began on September 29, 1947.

The program is administered by a joint committee of the School and the Hospital, known as the University Committee under the chairmanship of Mr. I. J. Goldberg, first vice-president of the Mount Sinai Hospital. When the affiliation is completed, the Mount Sinai Hospital of Chicago will become a University Hospital.

This association will benefit both institutions. It will not only elevate the standards of teaching both qualitatively and quantitatively, but will also improve medical care and enhance productive investigative work by the two institutions through the employment of full-time clinical professors. At the present time there are full-time appointments to the clinical teaching staff at Mount Sinai Hospital in medicine, surgery, dispensary, and a half-time appointment in psychiatry.

* * * * * *

The Chicago Medical School has established an office in New York City which is under the supervision of our trustee, Mr. Mark Sugarman, and Dr. Sidney Marks. It is located in the Medical Arts Building, 57 West 57th Street.

* * * * * *

Dean John A. Sheinin recently attended the meeting of the Association of American Medical Colleges held at Sun Valley, Idaho.

* * * * * *

At the annual meeting of the American Academy or Orthopedic Surgeons held at the Palmer House in January, Dr. Donald S. Miller described new techniques in the treatment of stubborn fractures utilizing the peripheral vascular system.

Surgeons should be very careful
When they wield the knife;
For underneath their fine incision
Lurks the culprit — Life!"

—Emily Dickinson

EDWIN O. FREUND

On November 12, 1947, there passed away a man who, despite his worldly gains, retained the common touch. He realized that a prime objective of a happy life was the aid and comfort of his fellow men.

Mr. Edwin O. Freund began his career as an office boy in 1907. By 1926 he had formed the Visking Corporation, the first producers of the seamless cellulose sausage casings, which is today a thriving industry.

Mr. Freund was a generous benefactor of the Chicago Medical School as well as a member of our Board of Trustees. His other philanthropic activities included interest in the United Negro College fund and the Jewish Children's Bureau.

The Board of Trustees of Chicago Medical School, upon learning of the death of their fellow member, sent the following letter to his family:

"November 18, 1947

Dear Mrs. Freund:

The Board of Trustees of the Chicago Medical School spread upon its minutes the following resolution:

'Be it resolved, that the Board of Trustees of the Chicago Medical School gratefully acknowledges the deep interest and the benefactions of Mr. Edwin O. Freund on behalf of the Chicago Medical School; that the Board of Trustees pays tribute to the memory of a great civic leader, an altruistic benefactor, and a human being of the first magnitude.

'Be it further resolved, that the sympathy of this board be conveyed to the family of the late Mr. Freund.'

The Board values deeply the devotion and the untiring efforts which Mr. Freund expended so generously in the alleviation of human suffering and the fostering of the doctrine of love and service for our fellow-man.

Very sincerely yours,
(signed) Henry A. Smith, M D.
Secretary, Board of Trustees"

We all deeply regret the death of our trusted friend, a man we all loved and respected, Mr. Edwin O. Freund.

IN MEMORIAM

EDWIN O. FREUND

In memory of Mr. E. O. Freund, an enlargement of this photograph will be placed in the library of the Chicago Medical School.

ELIAS SELINGER

We deeply regret the untimely passing of Dr. Elias Selinger, who suddenly succumbed while en route to California where he was going for his health.

Though only 49 years old, Dr. Selinger accomplished much during his lifetime. Graduated from Northwestern University Medical School, he took a residency in Cook County Hospital and post-graduate work in opthalmology abroad. He taught at Northwestern University and Rush Medical Schools for 15 years before coming here and was attending ophtalmologist at Cook County, Michael Reese and Mount Sinai Hospitals. A member of the American Board of Ophalmology, he was also a member of numerous other societies, published many papers and wrote a book "Office Treatment of the Eye," which was published shortly before his death.

Although he was with us but a short time, Dr. Selinger brought with him new heights in teaching.

* * *

NEW FACULTY ADDITIONS

Israel Davidsohn, M.D.

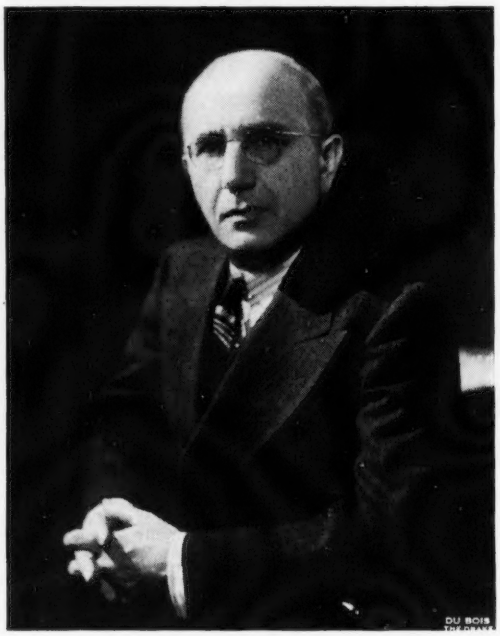
In choosing a chairman of the Department of Pathology, the Chicago Medical School was faced with the problem of finding a man who was well known in his field, a man who has established himself as an authority, and a man who could and would organize the pathology department into the finest teaching department in the city. These prerequisites have all been fulfilled in the person of Dr. Israel Davidsohn.

Evidence of Dr. Davidsohn's prominence in his field is provided by the following of societies to which he belongs:

American Medical Association
College of American Pathologists
American College of Physicians
Chicago Medical Society
Institute of Medicine of Chicago
Chicago Pathological Society
Society of Medical History of Chicago
Illinois Medical Society
Illinois Society of Pathologists
Illinois Society of Bacteriologists
American Association of Pathologists and Bacteriologists
American Society of Clinical Pathologists
International Association of Medical Museums
American Society of Experimental Pathology
Society for Experimental Biology and Medicine
American Association of Immunologists
American Association for Advancement of Sciences
Diplomate of The American Board of Pathology and Clinical Pathology

He is the author of 52 articles appearing in various medical journals—the subjects of which are too numerous to mention in the limited space available. However, we will mention some of the books he has written. They include:

1. "A Curriculum for Schools of Medical Technology"—2nd Edition—1942.
2. Co-author of Downey's "Handbook of Hematology", especially the chapter on the *Serologic Diagnosis of Infectious Mononucleosis.*
3. Co-author of Kracke's "A Textbook of Clinical Pathology" and the chapter on *Serologic tests for Syphilis.*
4. Co-author of Kolmen and Boerner's "Approved Laboratory Technic", especially the chapters on *Methods of Conducting Hemagglutination and Blood Grouping Tests,* and *Methods for the Examination of the Blood and Urine for Hormones.*



Dr. Israel Davidsohn

5. Co-author of Bachmeyer and Hartmann's "The Hospital in Modern Society", especially the chapter on *Management of Laboratories.*

Dr. Davidsohn was born in Tarnopol, Austria on April 20, 1895. He attended the University of Vienna Medical School and did postgraduate work there and at the University of Berlin. He came over to the United States in 1923 and took an internship at Mount Sinai Hospital in Philadelphia. He also took his resident training there and soon became pathologist and Director of Laboratories of this hospital. After completing his work at Philadelphia's Mt. Sinai Hospital, he became a Fellow of the Research Institute of Cutaneous Medicine. In 1930, the doctor moved to Chicago and assumed the position of pathologist and Director of Laboratories of Mount Sinai Hospital in Chicago.

Dr. Davidsohn was formerly an Associate Professor of Pathology at the College of Medicine of the University of Illinois. Among his other attainments he counts being the former editor of the American Journal of Clinical Pathology and the Technical Bulletin. He is also a surgeon in the Reserve of the United States Public Health Service and is now the chairman of the department of Pathology of the Chicago Medical School.

* * * * *

Ernest Loeffler, M.D.

We, of the QUARTERLY and of the school are very happy to welcome back to our Pathology Department, Dr. Ernest Loeffler. Dr. Loeffler taught at C.M.S. from 1939 to 1943, and it was our misfortune to lose his services up to the present time. However, now that he has returned our Pathology Department has improved greatly.

Dr. Loeffler was born in Hohenelbe, Austria and went to the University of Vienna Medical School for his degree. After his graduation in 1917, he worked at the Pathological Institute in Rudolpfpital, Vienna. After working here, he became assistant pathologist in the Pathological Institute of the University of Vienna and in the Pathological Institute of the Hospital of the city of Vienna. From 1925 till the time of Hitler's "Anschluss" with Austria, Dr. Loeffler was the Pathologist at three of the city hospitals in Vienna.

In 1939, Dr. Loeffler came to the United States and became Assistant Professor in the Chicago Medical School's Department of Pathology. Among other honors, he is a diplomate of the American Board of Pathology. After he left C.M.S., he became Assistant Pathologist at Mt. Sinai Hospital in Chicago and Senior Pathologist at Cook County Hospital. Dr. Loeffler's later affiliation is with C.M.S. and we hope he is as happy to be here as we to have him back.

Dr. Ernest Loefler

* * * *

Morris Goldenberg, M.D.

To round out the finest Pathology Department in C.M.S. history we have acquired the services of Dr. Morris Goldenberg. Dr. Goldenberg took his degree at the University of Iowa College of Medicine in 1939 and interned at Edgewater Hospital from 1939 to 1940. Dr. Goldenberg soon realized that his love of Pathology was more than just a passing fancy and therefore he took a post-graduate course and a residency at Cook County Hospital. This post-graduate training took three years and soon after completing this work he rendered his services to the Army.

The doctor saw service with the 132nd General Hospital in the Southwest Pacific Theater. He attained the rank of major and later became Pathologist and Commanding Officer of the 363rd

Medical Laboratory. He was in the armed services for four years and was honorably discharged in May of 1946. The doctor then returned to Cook County Hospital and resumed his residency for one more year.

Dr. Morris Goldenberg

Doctor Goldenberg has hospital affiliations with the South Chicago Community Hospital and has passed his American Boards in Pathological Anatomy and Clinical Pathology. Other than hospital affiliations, the doctor has been associated with the following medical societies and organizations:

Chicago Medical Society
American Medical Association
Illinois State Medical Society
Chicago Pathological Society
American Society of Clinical Pathologists.

* * *

Benjamin H. Nieman, M.D.

The Autopsy course at Cook County Hospital is one of those courses in medical school that seems to organize the previous didactic work of a student into something tangible, which can then be applied to the clinical work ahead. The task of preparing our students has been delegated to the very capable hands of Dr. Benjamin H. Nieman.

Dr. Nieman was born in Toronto, Ontario, Canada, and came to the United States in 1916. He attended the University of Chicago and in 1926 received his Bachelor's degree. In 1930 he received his Medical degree from The Rush Medical College and then went to the University of Illinois to take his Master's degree.

He interned at Cook County Hospital and also took a residency in Pathology for five years. Dr. Nieman was formerly an instructor in Anatomy and Pathology at the University of Illinois. When the war started, Dr. Nieman served with the Loyola Unit which was known as the 108th General Hospital, in which he attained the rank of Lieut. Colonel in the United States Army.

The army is not the only organization that considers Dr. Benjamin Nieman a fine pathologist. Dr. Nieman is a Diplomate from the American Board of Pathology and is a Fellow of the College of American Pathologists and a Fellow of the American College of Physicians and Surgeons. He also is the director of the Scientific Pathologic Laboratories and Pathologist at Macneal Memorial Hospital, American Hospital, and St. Joseph's Hospital in Joliet, Illinois.

Dr. Benjamin H. Nieman

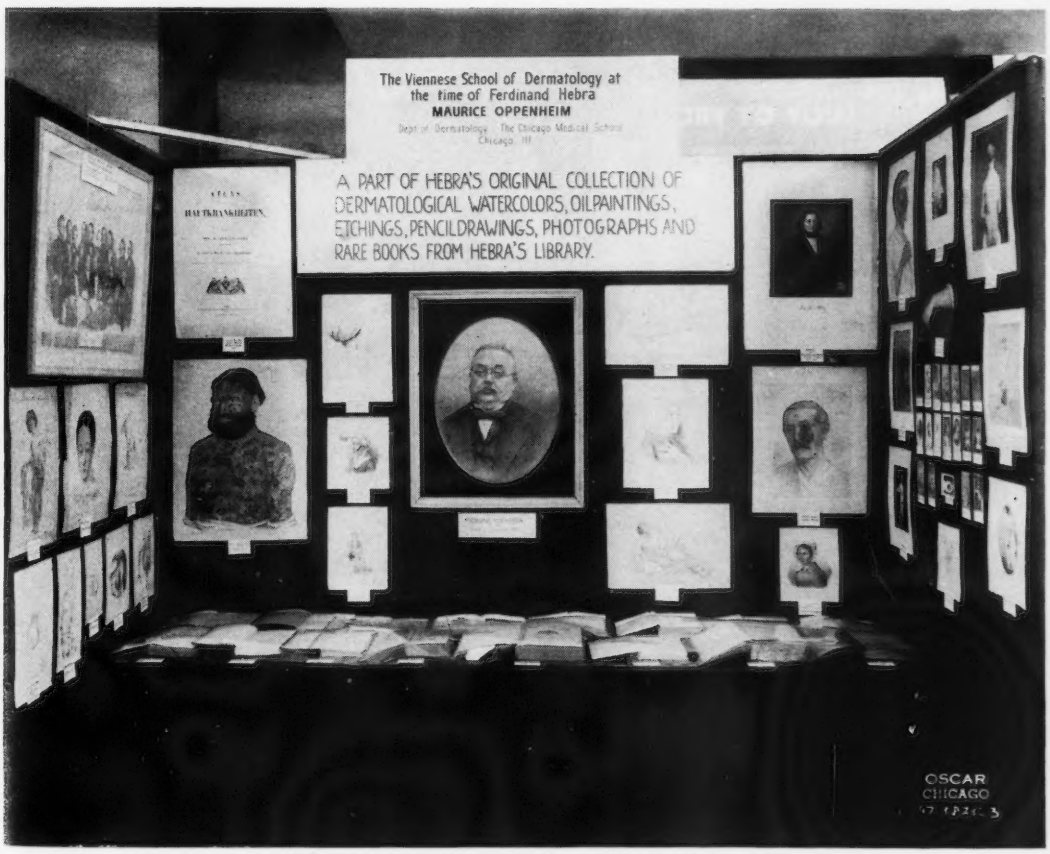
The exhibit of the American Academy of Dermatology and Syphilology from the 6th to the 11th of December 1947, at the Palmer House in Chicago; of the Department of Dermatology of The Chicago Medical School, arranged by Dr. Maurice Oppenheim, under the title, "The Viennese School of Dermatology at the Time of Ferdinand von Hebra," by Dr. Maurice Oppenheim, Head of the Dermatology Department.

The Dermatology Department of The Chicago Medical School exhibited the collection of Dr. Maurice Oppenheim, Professor of Dermatology and Syphilology of The Chicago Medical School at the Convention. For this, he received the honorable mention awarded by the academy.

One of the founders of modern Dermatology and among its greatest was Ferdinant von Hebra.* He inaugurated the anatomic-pathological concept and liberated Dermatology from the shackles of Internal Medicine giving it equal status with other specialties. Hebra was born in Moravia in 1816. He was graduated from the University of Vienna in 1841 and entered the Allgemeine Krankhaus the following year as an assistant physician of Joseph Skoda who was professor and head of Internal Medicine at the above hospital. At that time all skin cases were considered dyscrasias or disturbances of body fluids particularly of the blood, hence were admitted to the department of internal medicine. Hebra formed another important association with Carl Rokitansky, the father of modern pathology. Guided by these two men he applied the pathological observation to skin disturbances. These three brilliant stars in the sky of the Viennese School, the fathers of their respective fields of medicine (1840-1890) attracted to it doctors, students and patients from all corners of the earth.

One of the first papers Hebra wrote concerned

* William Allan Pusey, History of Dermatology, Chicago, 1943.



itself with Scabies. He believed it to be in the beginning a systemic disease but this concept was abandoned when he discovered that Acarus Scabiei or Sarcoptes Hominis (first described by Italian physician, Bonomi, almost two hundred years ago) was the causative agent. In the light of this discovery Hebra recognized that many skin disorders were expressions of local and external causes. By applying external stimulations, Hebra found that all the symptoms of skin inflammation could be reproduced. Thus he could discover and describe the nature of many skin disorders, eczema marginatum, erythema multiforme, impetigo herpetiformis, rhinoskleroma, prurigo, etc. His classification of skin diseases, although more than one hundred years old is still in use. The monumental "Atlas der Hautkranktenban" appeared between 1856-1876. His "Lehrbuch de Hautkrankheiten" was a standard work which was translated into almost every language.

Aside from innumerable contributions to Dermatology, Hebra was in addition a man of humor and courage. His witticisms will always bear repetition. I may mention as proof of his great personality the fact that he, together with Rokitansky and Skoda, defended a young Viennese physician, Ignatz Philipp Sommelweis, who propounded the contagiousness of puerperal fever; a view similarly held at that time by Oliver Wendell Holmes in the United States. Even Virchow opposed him. As a result, Sommelweis was forced to leave Vienna after his book "Etiology Concept and Prophylaxis of Puerperal Fever" was published in 1861 and he subsequently died in an insane asylum. Hebra died in 1880 at the age of 64; his students disseminating his concepts throughout the world. His most famous Viennese pupils were Moritz Koposi (1837-1898), Heinrich Auspitz (1835-1886), and my teacher, Isador Neumann (1832-1906).

I want to thank Dr. William Yacullo, Dr. Sidney Bazell, and my daughter Ridi Spiesman for helping me in the arrangement of the exhibit.

Correction: William Allen Pusey, History of Dermatology; W. C. Thomas & Co., Springfield, Ill., 1933.

* * *

NEW FACULTY MEMBERS

Byron L. Robinson, M.D., Associate Professor in Anatomy

Harold Somers Fish, Ph.D., Associate Professor in Anatomy

George Clark, Ph.D., Associate Professor in Anatomy

Leon Henri Strong, Ph.D., Assistant Professor in Anatomy

George J. Scheff, M.D., Ph.D., Assistant Professor in Microbiology

Ernest Hartman, Sc.D., Assistant Professor in Parasitology

Leo J. Saidel, Ph.D., Instructor in Biochemistry

PUBLICATIONS

Koppers, P. H.: An atypical strain of pseudomonas aeruginosa. Jour. Bact., Vol. 53, No. 3, September 1947.

Koppers, P. H. & Beard, H. H.: Creatinase activity of a strain of pseudomonas. Arch. Biochem., Vol. 15, No. 2, November 1947.

—MEDICAL TID-BITS—

Patients in the Veterans' Administration Hospital at Martinsburg, W. Va., can learn to develop photographs while still bedridden. The hospital's pre-vocational Shop Retraining division obtained a supply of Devolite photographic printing paper, which has such a slow exposure factor that it can be used for making contact prints in the daylight.—*Current Medical Digest*, September 1947.

* * * * * *

Keep the faculty of effort alive in you by a little gratuitous exercise every day. That is, be systematically ascetic or heroic in little unnecessary points, do every day or two something for no other reason than that you would rather not do it, so that when the hour of dire need draws nigh, it may find you not unnerved and untrained to stand the test.

—William James

Peripheral Vascular Disorders—

(Continued from page 6)

expose the extremity to continuous cooling or to room temperature. The evidence appears to be somewhat in favor of the latter procedure. There is some proof to indicate that it is advisable to remove vasoconstriction through various procedures, such as the use of Dibenamine, repeated paravertebral sympathetic blocks, and if these produce a therapeutic effect, then by sympathectomy.

Alumni News

Several hundred alumni were present at the Sherman Hotel on December 19, 1947, when Dean John J. Sheinin gave a smoker for the first class reunion of the alumni of the Chicago Medical School. The guest speaker was Prof. Leslie Brainerd Arey, Chairman, Department of Anatomy of the Northwestern University Medical School.

The audience was also addressed by Dr. Sheinin, Dr. Henry A. Smith, President of the Alumni Association, and Dr. Rudder, Chairman of the Endowment Committee of the Alumni Association.

* * * * *

A series of symposia and lectures are being planned for the alumni that is intended to achieve a twofold objective: (1) to promote a closer relationship between our alumni and the School, and (2) to present information concerning the progress of the medical sciences. In order to obtain their individual views, personal wishes and interests in this respect, a questionnaire has been mailed to the alumni.

* * * *

1908

We are sorry to hear of the death of **Leopold Sanford Gumberts,** Jenner 1908, who died April 27, 1947, at the age of 83.

1910

The Quarterly has also received news of the death of **Nicholas J. Jackson,** of Jenner 1910.

1921

Bad news is also received from the Class of 1921, on the death of **Andrew J. Erickson,** formerly of 843 No. Pine St., Chicago.

1931

Dr. Thomas Joseph Moran of Alton Illinois died at the Alton Memorial Hispital where he was a member of the staff, on December 14, 1946, aged 48, of cerebral hemmorhage. He was also affiliated with St. Joseph's Hospital. (From Ill. Med. Journal, May 1947.)

1938

The Quarterly wishes to thank **Dr. James E. Segraves** for his generous contribution to The Quarterly.

1940

Mr. and Mrs. Clyde Spann announce the marriage of their daughter Leila Doris to **Dr. Herman J. Horovitz** on May 25, 1947.

1942

The stork was busy at the Hootnick home when Shirley Diane honored **Dr. and Mrs. Harry L. Hootnick** with her appearance on July 4, 1947. Let's hear more good news from the Class of '42.

1943

Dr. Arthur Howard announces the opening of his office at 2227 W. Main Street, Johnstown, New York. Dr. Howard would appreciate letters from old classmates.

1945

Dr. and Mrs. Roy A. Hecht kept up the birthrate of the Class of '45 when they proudly exhibited a son, Ronald Anthony, on June 8, 1947.

On March 6, 1947, Wesley Forrest Byloff made his parents, **Dr. and Mrs. Forrest G. Byloff,** proud parents by being delivered by a stork, or doctor, or something.

Just to show that the Class of '45 is right in there pitching, **Dr. and Mrs. Arthur Light** became parents of a son, Terry Richard, on June 22, 1947.

Dr. Samuel Kahan announces the opening of his office at 3154 W. Diversey Blvd., Chicago, Ill.

Dr. Max Rothman writes telling us that he is on the staff of Utica State Hospital training for his Boards in Psychiatry. He tells us that the New York State Hospital has many opportunities opened to those interested in psychiatry.

Dr. Bernard Galston and Miss Marilyn Glick became husband and wife on December 7, 1947, at the Blackstone Hotel, Chicago.

1946

Mr. and Mrs. Zelik Rozmarin announce the bethrothal of their daughter, Dee, to **Dr. Max Linderman,** son of Mr. and Mrs. William Linderman. Many thanks for the announcement. We are sure the Class of '46 will get the news.

The program read as follows:

Premiere Performance — Jamaica Hospital, Sept. 11, 1947, etc. In it we were also told that **Dr. and Mrs. Murray M. Feldman** de-

signed the production of "Life With Baby" starring Eileen Theresa. We must mention that the program states that Costumes are subject to change without notice.

The Class of '46 will soon be doing what the Class of '45 has done . . .

Mr. and Mrs. Edwin S. Flarsheim announced the marriage of their daughter Jane to **Dr. Theodore Thomas Blumberg** on July 20, 1947, from Cincinnati, Ohio.

Dr. and Mrs. Harry William Helman announced the marriage of their daughter, **Normabelle (Dr. Normabelle Helman)** to Mr. John Cuthbert Shivley on July 5, 1947.

1947

We had to read the engagement cards twice before we realized that Mr. and Mrs. Isidore L. Silverman announced the engagements of their twin daughters to **two** CMS graduates. **Dr. Irving Shonberg to Emilee** on June 16, 1947, and **Dr. Jerome A. Ehrlich** to Francine on August 22, 1947.

ALUMNI RECENTY SEPARATED FROM SERVICE

Dr. Mario A. Accinno	CMS 1938
Dr. Milton Dillon	CMS 1944
Dr. Jules L. Harran	CMS 1944
Dr. Philip Kavet	CMS 1944
Dr. Edward D. Nisson	CMS 1944
Dr. Raymond S. Rowlette	CMS 9145
Dr. Bart D. Iaia	CMS 1945

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— MEDICAL TID-BITS —

Moore defines three types of "cure" in syphilis: (1) Biologic "cure" signifies that the patient's body has been completely sterilized of Treponema pallidum; (2) Symptomatic "cure" implies that all symptoms and signs of the disease have disappeared; the patient remains well and non-infectious; (3) Serologic "cure" refers solely to a permanent reversal of positive blood and cerebrospinal fluid tests. The attainment of biologic "cure" obviously implies that symptomatic and serologic "cure" has occurred. Serologic "cure" should in no sense be confused with biologic or symptomatic cure. It is occasionally associated with active, progressive disease.

—Modern Medical Therapy

Psychiatrist: The thing for you to do is to stop thinking about yourself—bury yourself in your work.

Patient: Gosh—and me a concrete mixer.

Post-operative peritonitis after a gastric resection killed Hortense Bentley. That was 18 months ago. Mr. Bently married her sister and last night she, too, succumbed to the same affliction. Mr. Bently telephoned to the undertaker, "Please arrange for the funeral of my wife. She just passed away." "Your wife!" screamed the undertaker, why, I buried her a year and a half ago." The husband weepingly explained that he had married again. 'Oh," came from the mortician. "I didn't know it. Congratulations." — *Roche Review,* October 1947.

* * * * *

Jones: I like that country—it's very healthy. All the time I was out there I never paid a doctor bill.

Wilson: I know that; I met the doctor and he told me.

—The Doctor

DEAR DOCTOR:

This magazine is intended for you. We hope you like it and the succeeding issues.

Publishing a medical journal is a costly affair; and we cannot accept many advertisements. Will you help us, and at the same time, yourself, by remitting your subscription as quickly as feasible?

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(2 year's subscription, $3.00)

Dr..... Class of .....

.....

.....

—MEDICAL TID-BITS—

"Os sacrum, the 'sacred' bone—called 'Luz' in ancient times—(was) supposed to be able to resist decay and to be the seed from which the body is resurrected."—*Cunningham's Textbook of Anatomy.*

"Until 1743, surgeons (in France) were . . . officially associated with the barbers and wigmakers in the 'Barber-Surgeons' Guild'. In 1802, Larrey presented a thesis on 'Amputations' to the Faculty of the School of Medicine in Paris, and was the first to receive the new title of 'Doctor of Surgery'."—Fanny J. Anderson, *Journal of the History of Medicine,* April 1946.

Diseases of the heart and arteries killed more than 536,000 persons in 1940, but only $93,835.00 was spent that year on research on these diseases. By contrast, $2.18 research money was spent for each of the 164,906 cancer deaths, $4.00 for each death from infectious disease other than infantile paralysis, and $525.00 for each of the 1,026 infantile paralysis deaths or $100.00 for each case dead or seriously crippled.

—Rhode Island J. Med.

One or more relapses will occur in about 60% of all cases of those persons who have had benign malaria (of the tertian or quartan types).

Nearly 60% of the total infantile fatalities occur within the first 24 hours. The causes are: congenital anomalies and intermitten cyanosis. Moderate anoxia may also cause fetal asphyxia.

Gizzards in birds, in which the food swallowed is ground up, working in conjunction with powerful gastric juices, perform amazing feats; sea ducks, for example, swallow whole crustaceans, and reduce the shells to five sands.

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Volume 2, Number 2
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